

# Proadrenomedullin as a prognostic biomarker for critically-ill septic children

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## Research article

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# Abstract

**Background:** The use of new biomarkers is a promising tool to assess risk of mortality among septic children. The aim of the study was to confirm prognostic and diagnostic value of pro-ADM as a marker in critically ill septic children.

**Methods:** This study was conducted on 40 patients who were admitted at pediatric intensive care unit (PICU), diagnosed as sepsis in addition to 40 patients enrolled as control group. Serum pro-ADM level was measured for both cases and controls.

**Results:** The level of pro-ADM was significantly higher in cases than controls (p-value <0.001). However, no correlation between level of pro-ADM and outcome (p value 0.720) was found.

**Conclusion:** The pro-ADM level was higher in cases than control, thus proved its diagnostic value but can't be used as prognostic factor. Future studies are recommended and daily measurements are warranted to study its prognostic value.

## Background:

Sepsis is among the commonest causes of mortality in hospitals. New sepsis biomarkers are needed to help in therapeutic decision making, screening, diagnosis, risk stratification, and monitoring of response to therapy in PICUs (1).

Risk scores such as Pediatric Risk Mortality Score (PRISM III), Pediatric Multiple Organ Dysfunction Score, Sepsis-Related Organ Failure Assessment and Pediatric Logistic Organ Dysfunction (PELOD) have been the best tools to estimate the prognostic and mortality risk in the first 24 hours of critical children (2). Blood cultures are positive in about 50% of patients with severe sepsis/septic shock (3).

Adrenomedullin (ADM) is a 52 amino acids comprising peptide derived from a larger precursor (pre-pro-ADM, 185 amino acids) by post-translational processing (4). Its actions include immune modulating, metabolic and vascular actions. It is also a vasodilator, and so helps to maintain blood supply to individual organs (5). It has also bactericidal activity. ADM serum levels increase in sepsis (6).

The measurement of ADM is technically difficult being rapidly cleared from circulation (short half-life of 22 minutes). Circulating ADM is masked by binding protein (complement factor H), making it inaccessible for immunometric analysis (5).

The mid-regional fragment of pro-adrenomedullin (MR-pro-ADM), comprising amino acids 45–92, is more stable. It reflects levels of the rapidly degraded active peptide ADM, and was identified in plasma of septic shock patients (7).

The aim of our study was to confirm prognostic and diagnostic value of proadrenomedullin marker in critically-ill septic children and to compare its prognostic usefulness to other biomarkers as C-reactive

protein (CRP).

## Methods:

This was a prospective observational study conducted on patients with sepsis admitted to pediatric intensive care units (PICUs) in Cairo University Children Hospital during 6 months interval from January 2016 to July 2016.

A total of 80 participants were included in the study; Group 1: 40 patients (1 month to 12 years) diagnosed with sepsis and requiring PICU stay and Group 2: 40 age and gender-matched healthy children as a control group. The diagnosis of sepsis was confirmed according to the International guidelines of sepsis (8).

Children with immediate postoperative cardiac surgery, chronic lung disease and immunodeficiency were excluded from the study. These pathologies were excluded because they may affect circulating ADM.

Full history taking (including age, sex and original diagnosis) and Clinical examination for all patients was recorded including; vital signs [heart rate, respiratory rate, temperature (low grade fever is defined as temperature  $< 38.5$  and high grade fever as temperature  $> 38.5$ ) and blood pressure], capillary refill time [considered normal up to 2 sec], pupillary reaction, urine output over 24 hours [normal range 1 to 3 ml/kg/hour] and Glasgow coma scale.

Grading of sepsis was reported according to international guidelines of sepsis into infection, systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, septic shock and multi-organ dysfunction syndrome (MODS) (8).

Routine laboratory investigations were done and included complete blood count (CBC) [using using automated hematology coulter (Cell Dyne 3700, Abbott laboratories; North Chicago, USA)], C-reactive protein [using latex agglutination test] and blood chemistry including serum creatinine, aspartate transaminase, alanine transaminase, total serum calcium, bilirubin, glucose and potassium levels [using automated analyzer Hitachi 917; commercial kits were supplied by Roche diagnostics (Boehringer Mannheim, GmbH D-68298, Mannheim, Germany)] and arterial blood gases.

PRISM III was done for all cases (9). Inotropic score was measured [dopamine dose  $\mu\text{g}/\text{kg}/\text{min}$  + dobutamine dose ( $\mu\text{g}/\text{kg}/\text{min}$ ) + 100 epinephrine dose ( $\mu\text{g}/\text{kg}/\text{min}$ )] (10).

Pro-ADM serum level was done by Enzyme-linked immune-sorbent assay (ELISA).

## Principles of the assay:

The kit assay Human Pro-ADM level in the sample, Purified Human Pro -ADM antibody was used to coat microtiter plate wells, solid phase antibody was made, then pro-ADM was added to wells, combined pro-ADM antibody which with horseradish peroxidase (HRP) labeled, became antibody-antigen-enzyme-

antibody complex. After washing completely, tetramethylbenzidine substrate (TMB) solution was added. TMB substrate became blue color at HRP enzyme-catalyzed. Reaction was terminated by the addition of a sulphuric acid solution and the color change was measured spectrophotometrically at a wavelength of 450 nm. The concentration of pro-ADM in the samples was then determined by comparing the optical density of the samples to the standard curve.

## Statistical Analysis:

Data was analyzed by SPSS statistical package version 17. Excel computer program was used to tabulate the results, and represent it graphically. Quantitative variables were expressed as mean and standard error. Qualitative variables were expressed as count and percent.

One Way ANOVA was used to declare the significant difference between groups at  $p < 0.05$ . Duncan multiple comparison test at  $p < 0.05$  was used to declare the significant between each two groups. Chi square test used to declare the significant difference in the distribution between groups at  $p < 0.05$  (11).

## Results:

48 children (60%) were males and 32 (40%) were females. The mean age of cases was  $14.63 \pm 2.60$  months while the mean age of controls was  $16.22 \pm 2.84$ , with no statistically significant difference between the 2 groups ( $p = 0.718$ ).

High percentage of cases was diagnosed as pneumonia (29 patients, 72.5%), followed by gastroenteritis (4 patients, 10%), encephalopathy and postoperative infection (3 patients, 7.5%, each) and urinary tract infection with acute kidney injury (one patient, 2.5%).

Table (1) shows clinical data of the case group. Table (2) shows laboratory investigations done to the cases.

The mean inotropic score was  $6.75 \pm 2.74$ , the mean PRISM score was  $10.87 \pm 1.32$  and the mean Glasgow coma score was  $10.85 \pm 0.34$ .

According to severity of sepsis, 8 cases (20%) had SIRS, 9 cases (22.5%) had sepsis, 9 cases had severe sepsis (22.5%), 7 cases (17.5%) had septic shock and 7 cases (17.5%) had MODS.

Level of pro-ADM showed a statistically significant difference between cases (mean  $46.47 \pm 9.87$ ) and controls (mean  $5.73 \pm 0.20$ ) ( $p < 0.001$ ).

Figure (1) shows Receiver Operating Characteristic (ROC) curve analysis for pro-ADM, and revealed that the best cut-off value of pro-ADM was 8.4, sensitivity was 67.55 and specificity 95%.

Sixteen cases (40%) died during the study while 24 cases (60%) were discharged. Correlations between the level of pro-ADM and age and laboratory investigations in the case group revealed a positive correlation between pro-ADM and CRP level.

Table (3) shows correlation between outcome of cases and PRISM score, CRP, inotropic score and pro-ADM level. There were significant positive correlations between outcome and both PRISM and inotropic scores.

Table (4) shows correlation between different grades of sepsis and CRP. It shows statistically significant correlation between different grades of sepsis and CRP.

## **Discussion:**

Sepsis is a systemic inflammatory reaction triggered by an infective agent (12). Severe sepsis may result in systemic inflammation, multi-organ failure and septic shock. It is one of the major health problems all over the world and a common reason for intensive care unit (ICU) admission (13).

Infections and sepsis are accompanied by clinical signs such as changes in body temperature and tachycardia which are not sensitive or specific for sepsis. They have only moderate sensitivity and specificity and are not early markers due to the time taken to produce a reaction (14). General inflammatory markers such as leukocytosis and blood cultures together with CRP and procalcitonin (PCT) are commonly used to complement the diagnosis. ADM has been proposed as a useful biomarker for evaluating disease severity and risk of death (15).

Pro-ADM correlates well with other markers such as IL-6 (interleukin 6) and CRP as a predictor of prognosis in sepsis. In adults, elevations of pro-ADM were found in different stages of septic patients as systemic inflammatory response syndrome (SIRS), sepsis, and septic shock (4).

The 40 cases included in our study were classified into 8 cases (22.5%) with SIRS, 9 cases (22.5%) with sepsis, 9 cases (22.5%) with severe sepsis, 7 cases (17.5%) with septic shock and 5 cases (12.5%) with MODS.

On the contrary, Christ-Crain et al., 2006 (16) found that 53/101 patients (52.5%) had sepsis, severe sepsis or septic shock, while 48 patients (47.5%) had systemic inflammatory response syndrome. This means that our patients started coming to the hospital after reaching late stage of disease evolution.

Twenty four cases were males (60%) and 16 were females (40%) with no significant correlation between sex and level of proadrenomedullin.

Similarly Jordan et al., 2014 (17) found that 59/95 patients involved in their study were males (62%) and the rest were females. This revealed that incidence of sepsis is more common in males than females. This may be due to sex-related hormonal secretion, different patterns of pro-inflammatory and anti-inflammatory mediators in response to severe sepsis and more favorable hormonal and immunologic profile in females (18).

In our study, level of proadrenomedullin was significantly higher in cases than controls with p-value < 0.001.

This is in agreement with Oncel et al., 2012 (4), who revealed significantly higher levels of pro-ADM in cases with clinical and proven sepsis compared to healthy controls.

Also Christ-Crain et al., 2006 (16), measured pro-ADM in patients with different grades of sepsis and found that it was significantly higher in all sepsis groups compared to healthy controls or non-infected critically-ill patients.

A physiological explanation for the increase of circulating MR-pro-ADM could be because being a member of the calcitonin gene family, it is expressed and highly synthesized during sepsis similar to other calcitonin peptides such as PCT (19). In addition, bacterial endotoxins and proinflammatory cytokines may contribute to the upregulation of ADM gene expression in different tissues (20).

In order to prove the prognostic value of proadrenomedullin we correlated between its level, grades of sepsis (p-value 0.790), PRISM III score (p-value 0.6), outcome of patients either discharged or died (p-value 0.720) and inotropic score (p-value 0.616) but no correlation was found.

Similarly, Christ-Crain et al., 2006 (16), found that there was no significant difference between levels of ADM between patients with SIRS and those with sepsis.

On the contrary, Jordan et al., 2014 (17) reported higher median values of MR-pro-ADM levels in ventilated patients or in cases needing inotropic support and in mortality cases. MR-pro-ADM levels at admittance showed a significant positive correlation with PRISM III score ( $r = 0.447$ ;  $p < 0.001$ ).

Also Guignant et al., 2009 (21) who performed their study on septic adult patients, revealed that MR-pro-ADM levels were significantly higher in non survivors.

In our study, correlation between CRP and grades of sepsis revealed positive correlation as when increasing grade of sepsis, CRP increases (p-value 0.005) which proves better prognostic value than pro-ADM while by correlation between CRP and outcome of patients we did not find any correlation between them (p-value 0.262) similar to pro-ADM.

Against our study, Christ-Crain et al., 2006 (16) concluded the superior prognostic accuracy of MR-pro-ADM over other biomarkers such as CRP and PCT as the mean plasma MR-pro-ADM levels were significantly higher in non survivors.

Similar results were obtained by Hagag et al., 2011 (22), who found that pro-ADM was lower in survivors in contrast to non-survivor cases; on the other hand CRP was not significantly different between survivors and non-survivors.

Wang and Kang, 2010 (23), clarified that, on the first day of ICU admission, pre-atrial natriuretic peptide (pre-ANP) and pro-ADM in patients with sepsis, severe sepsis, or septic shock increased in non-survivors as compared with survivors, while other markers of infection and inflammation (CRP, IL-6 and PCT) were not which shows that pre-ANP and pro-ADM are better in predicting the severity of septic patients.

In our study, also by correlating between outcome and PRISM III, a significant correlation (p value 0.023) was found, as the higher the PRISM score, the incidence of mortality increases. Also a significant correlation was found between outcome and inotropic score (p-value 0.007), as the higher the inotropic score, the incidence of mortality increases. This showed that clinical evaluation by PRISM score and inotropic score can predict the outcome of patients.

Jordan et al., 2014 (17), suggested the combined use of PRISM III and ADM as predictors of mortality in pediatric patients.

Our study showed positive correlation between pro-ADM and CRP (p-value 0.01). This justifies the usage of second parameters for diagnosis as combination between pro-ADM and other biomarkers as CRP.

Oncel et al., 2012 (4) found that pro-ADM levels decrease rapidly compared to CRP suggesting that instead of being used alone, combination with conventional acute-phase reactants may be more useful to diagnose and follow-up patients with sepsis.

## **Conclusion:**

Pro-ADM is a good diagnostic biomarker for sepsis being higher in cases than controls. It cannot be used as prognostic factor as no correlation between its level and outcome. Clinical assessment of sepsis by PRISM III and inotropic scores have better prognostic assessment for prediction of outcome of cases.

Future studies including larger number of patients are recommended. Daily follow-up measurements are needed to validate prognostic value of pro-ADM. It is recommended to combine several parameters e.g. clinical status of patients, PRISM and inotropic scores.

## **Abbreviations**

ADM: adenomedullin

CBC: complete blood count

CRP: C-reactive protein

ELISA: Enzyme-linked immune-sorbent assay

HRP: horseradish peroxidase

IL-6 (interleukin 6

MODS: multi-organ dysfunction syndrome

MR-ADM: mid regional fragment of adrenomedullin

PCT: procalcitonin

PELOD: Pediatric Logistic Organ Dysfunction

PICU: pediatric intensive care unit

pre-ANP: pre-atrial natriuretic peptide

PRISM III: Pediatric Risk Mortality Score

ROC: Receiver Operating Characteristic

SIRS: systemic inflammatory response syndrome

TMB: tetramethylbenzidine substrate

## Declarations

- **Ethics approval and consent to participate**

This study was approved by the scientific committee of pediatrics department, Cairo University and ethics committee in Cairo University (I-061013) and was conducted in accordance with the University bylaws for human research. It conforms to the provisions of the Declaration of Helsinki in 2000. All legal guardians have given their informed written consent.

- **Consent for publication:** Not applicable” in this section
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- **Authors' contributions:**

All authors have contributed significantly and all authors are in agreement with the content of the manuscript.

**EG:** Participated in search in the literatures, followed the results, and prepared the final manuscript.

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**MK:** Participated in choice the issue of the study, followed the results and prepared the final manuscript.

**SA:** Msc of pediatrics. Participated in collecting data of the patients, followed the results and searched in the literatures.

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## References

- 1-Reinhart K, Bauer M, Riedemann NC and Hartog CS. New approaches to sepsis: molecular diagnostics and biomarkers. *Clin Microbiol Rev* 2012;25:609-34.
- 2-Lacroix J and Cotting J. Severity of illness and organ dysfunction scoring in children. *Pediatr Crit Care Med* 2005;6:126-34.
- 3-Ntusi N, Aubin L, Oliver S, Whitclaw A and Mendelson M. Guideline for the optimal use of blood cultures. *SAMJ* 2010;100:839-42.
- 4-Oncel MY, Dilmen U, Erdeve O, Ozdemir R, Calisici E, Yurttutan S, Canpolat FE, Oquz SS and Uras N. Proadrenomedullin as a prognostic marker in neonatal sepsis. *Pediatr Res* 2012; 72:507-12.
- 5-Eto T. A review of the biological properties and clinical implications of adrenomedullin and proadrenomedullinN-terminal 20 peptide (PAMP), hypotensive and vasodilating peptides. *Peptides* 2001;22:1693–711.
- 6-Martinez A, Pio R, Zipfel PF and Cuttitta F. Mapping of the adrenomedullin-binding domains in human complement factor H. *Hypertens Res* 2003;26:55-9.
- 7-Struck J, Tao C, Morgenthaler NG and Bergmann A. Identification of adrenomedullin precursor fragment in plasma of sepsis patients. *Peptides* 2004;25:1369-72.
- 8-Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL and Vincent JL. Surviving Sepsis

Campaign: international guidelines for management of severe sepsis and septic shock. *Crit Care Med* 2008;36:296-327.

**9-Singhal D, Kumar N, Puliye JM, Singh SK and Srinivas V.** Prediction of mortality by application of PRISM score in intensive care unit. *Indian Pediatr* 2001;38:714-9

Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11463958>

**10- Wernovsky G, Wypij D, Jonas RA, Mayer JE Jr, Hanley FL and Hickey PR .** Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants. A comparison of low flow cardiopulmonary bypass and circulatory arrest. *Circulation* 1995;92:2226-35.

**11-Bolton S and Bon C.** Pharmaceutical statistics: Practical and Clinical Applications, 5<sup>th</sup> ed. Broken Sound Parkway, NW. Taylor and Francis. 2009.

<https://doi.org/10.3109/9781420074239>

**12-Monneret G.** Immunology programs must include sepsis. *Science* 2010;328:1106-16.

**13-Arabi Y, Al Shirawi N, Memish Z, Venkatesh S and Al-Shimemeri A.** Assessment of six mortality prediction models in patients admitted with severe sepsis and septic shock to the intensive care unit: a prospective cohort study. *Crit Care* 2003;7:116-122.

Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12974979>

**14-Fried E, Weissman C and Sprung C.** Postoperative sepsis. *Curr Opin Crit Care* 2011;17:396-401.

**15-Christ-Crain M and Opal SM.** Clinical review: The role of biomarkers in the diagnosis and management of community-acquired pneumonia. *Crit Care* 2010;14:203-13.

**16-Christ-Crain M, Morgenthaler NG, Stolz D, Müller C, Bingisser R, Harbarth S, Tamm M, Struck J, Bergmann A and Müller B.** Pro-adrenomedullin to predict severity and outcome in community-acquired pneumonia. *Crit Care* 2006;10: 96.

**17-Jordan I, Comiero P, Balaguer M and Ortiz J.** Adrenomedullin is a useful biomarker for the prognosis of critically ill septic children. *Biomark Med* 2014;8:1065-72.

**18-Knoferl MW, Diodato MD, Angele MK, Ayala A, Cioffi WG, Bland KI and Chaudry IH.** Do female sex steroids adversely or beneficially affect the depressed immuneresponses in males after trauma-hemorrhage? *Arch Surg* 2000;135:425-33.

**19-Becker KL, Nylen ES, White JC, Müller B and Snider RH Jr.** Procalcitonin and the calcitonin gene family of peptides in inflammation, infection, and sepsis: a journey from calcitonin back to its precursors. *J. Clin Endocrinol Metab.* 2004;89:1512–25.

**20-Linscheid P, Seboek D, Zulewski H, Keller U and Müller B.** Autocrine/ paracrine role of inflammation-mediated calcitonin gene related peptide and adrenomedullin expression in human adipose tissue. *Endocrinology*2005;146:2699-708.

**21-Guignant C, Voirin N, Venet F, Malcus C, Bohé J, Lepape A and Monneret G .** Assessment of pro-vasopressin and pro-adrenomedullin as predictors of 28-day mortality in septic shock patients. *Intensive Care Med* 2009;35:1859–67.

**22-Hagag A, Elmahdy HS and Ezzat AA.** Prognostic value of plasma Pro-Adrenomedullin and anti-thrombin levels in neonatal sepsis. *Indian Pediatrics*2011;48:471-3.

**23-Wang R and Kang F.** Prediction about severity and outcome of sepsis by pro-atrial natriuretic peptide and pro-adrenomedullin. *Chin J Traumatol*2010;13:152-7. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20515592>

## Tables

**Table (1): Clinical data of cases:**

		<b>cases</b>	
		<b>Count</b>	<b>%</b>
<b>Heart Rate</b>	<b>Bradycardia</b>	<b>1</b>	<b>2.5%</b>
	<b>Normal</b>	<b>13</b>	<b>32.5%</b>
	<b>Tachycardia</b>	<b>26</b>	<b>65.0%</b>
<b>Blood Pressure</b>	<b>Hypotensive</b>	<b>6</b>	<b>15.0%</b>
	<b>Normal</b>	<b>20</b>	<b>50.0%</b>
	<b>Hypertensive</b>	<b>14</b>	<b>35.0%</b>
<b>Temperature</b>	<b>Normal</b>	<b>16</b>	<b>40.0%</b>
	<b>Low Grade Fever</b>	<b>17</b>	<b>42.5%</b>
	<b>High Grade Fever</b>	<b>7</b>	<b>17.5%</b>
<b>Respiratory Rate</b>	<b>Normal</b>	<b>6</b>	<b>15.0%</b>
	<b>Tachypnic</b>	<b>34</b>	<b>85.0%</b>
<b>Capillary Refill</b>	<b>Normal</b>	<b>34</b>	<b>85.0%</b>
	<b>Prolonged</b>	<b>6</b>	<b>15.0%</b>
<b>Urine Output</b>	<b>Normal</b>	<b>37</b>	<b>92.5%</b>
	<b>Oliguric</b>	<b>3</b>	<b>7.5%</b>
<b>Pupils</b>	<b>Equal and reactive</b>	<b>34</b>	<b>85.0%</b>
	<b>Dilated and reactive</b>	<b>4</b>	<b>10.0%</b>
	<b>Dilated and irreactive</b>	<b>2</b>	<b>5.0%</b>

Table (2): Different laboratory investigations done for cases.

	Mean ± SE	Range
TLC (10 <sup>3</sup> / μL)	17.70 ± 1.91	5.400-54.000
Platelets (10 <sup>3</sup> / μL)	274.80 ± 30.86	2.000-649.000
CRP (mg/L)	53.96 ± 8.81	6-170
Creatinine (mg/dl)	0.57 ± 0.06	0.2-1.69
Total Billirubin (mg/dl)	1.94 ± 0.43	0.2-13
ALT (unit/dl)	111.30 ± 24.72	7-648
AST (unit/dl)	139.95 ± 29.51	26-693
Calcium (mg/dl)	8.60 ± 0.19	6.7-12.2
Glucose (mg/dl)	172.40 ± 20.31	70-484
Potassium (mEq/L)	3.81± 0.15	1.9-5.5

TLC: Total leucocytic count      CRP: C-reactive protein

ALT: Alanine transaminase      AST: Aspartate transaminase

**Table (3): Correlation between outcome with PRISM score, CRP, inotropic score and pro-ADM:**

	Outcome		P-value
	Discharged	Died	
	Mean ± SE	Mean ± SE	
PRISM Score	8.04±1.15	15.12±2.51	0.023
CRP (mg/L)	44.75±9.78	67.78±16.23	0.262
Inotropic Score	1.25±0.92	15.00±6.27	0.007
Pro-ADM (ng/L)	53.35±15.19	35.97±9.6	0.720

CRP: C-reactive protein

Pro-ADM: Pro-adrenomedullin

**Table (4): Correlation between different grades of sepsis and CRP:**

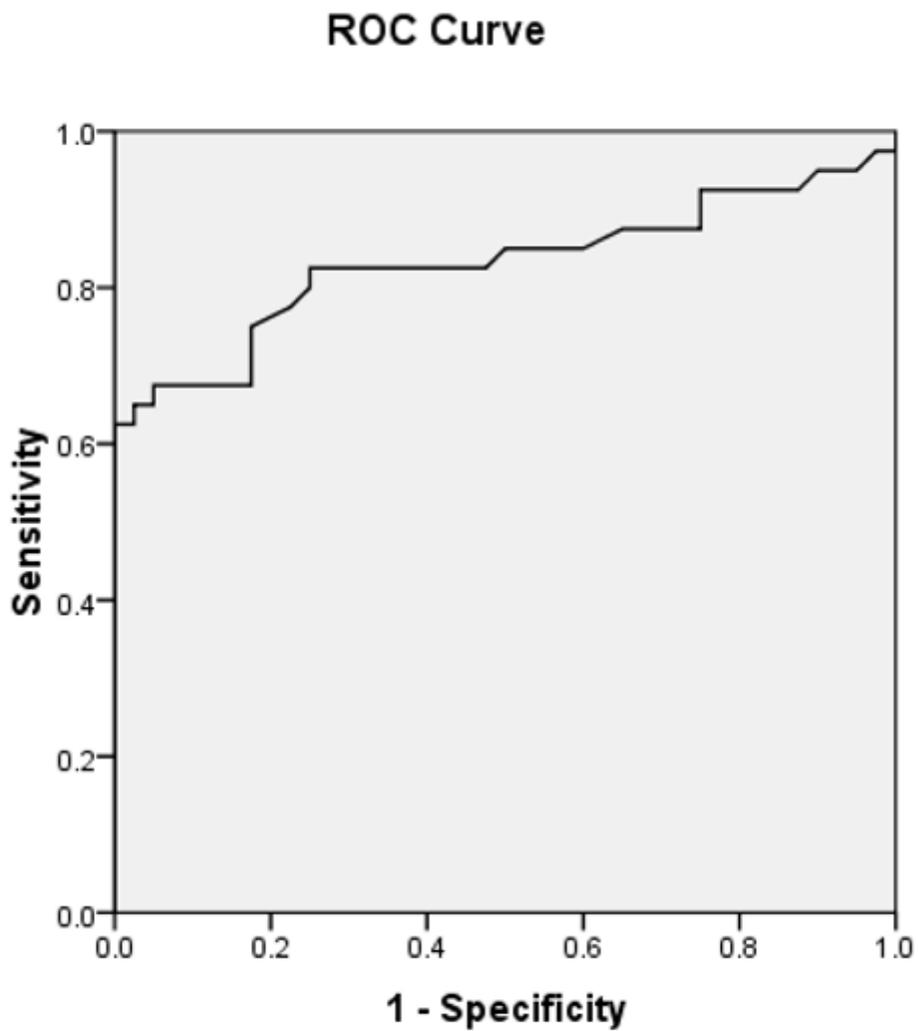
	Grade of Sepsis					P-value
	SIRS	Sepsis	Severe Sepsis	Septic shock	MODS	
	Mean ±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	
<b>CRP (mg/L)</b>	17.12±4.80	79.43±14.73	26.50±6.54	110.57±28.66	42.00±21.65	0.005

CRP: C-reactive protein

SIRS: Systemic inflammatory response syndrome

MODS: multi-organ dysfunction syndrome

## Figures



Diagonal segments are produced by ties.

**Figure 1**

ROC curve of pro-adrenomedullin. ROC: Receiver Operating Characteristic (ROC) curve.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [STROBEchecklistcasecontrol1.doc](#)