

ASSOCIATION BETWEEN PRO BRAIN NATRIURETIC PEPTIDE AND LENGTH OF STAY IN PATIENTS WITH SEPSIS.

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ABSTRACT

INTRODUCTION: Sepsis is the third major cause of mortality worldwide, with heart disease and cancer ranking first and second respectively. N-terminal pro-Brain Natriuretic Peptide (NT-proBNP) is a cardiac-overload biomarker associated with cardiovascular disease and sepsis severity^{3,4}. This study was conducted to discover the prognostic significance of proBNP in patients with sepsis but no evidence of heart disease, with respect to length of hospital stay. **METHODS:** Patients admitted to Dubai Hospital between August 2017 and April 2019, with a diagnosis of sepsis or septic shock and without any prior history of cardiac illnesses, were included in this study. ProBNP levels were tested within 48-72 hours of admission and results were analysed to look for its prognostic value in terms of length of hospital stay. Cross tabulation using Fisher's exact score was carried out between proBNP level, categories of PCT level and ethnicity of patient's with length of stay. Data was analysed retrospectively using SPSS software. **RESULTS:** A total of 48 patients were analysed. 67% were males and 33% were female. The median age was found to be 72.5 years. 58% of patients were from the Middle East and Africa (MENA) region, 35% from Asia, 4% from Europe and for 3% ethnicity was not recorded. 4.2% of the patients had normal levels of Pro-BNP, 16.7% had moderate levels and 79.2% had markedly high range. 25 % of the patients had mild levels of PCT, 17% had moderate levels, and 58% had markedly increased levels of PCT. 6.3% of patients discharged within 72 hours, 81.3% got discharged after 72 hours and 12.5% of the patients deceased during hospitalization. This study was unable to establish a significant relation between pro-BNP levels and length of hospital stay ($p=0.279$). Statistically significant relation was found between ethnicity and length of hospital stay with a p-value of 0.04. **CONCLUSION:** This study did not show strong association between proBNP and prognosis in terms of length of hospital stay in septic patients in the absence of previous cardiac diseases.

KEYWORDS: Sepsis, ProBNP, Shock, Septic Shock, BNP, Brain Natriuretic Peptide, Prognosis, Outcome

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INTRODUCTION

According to the Centre of Disease Control (CDC); around 1.7 million adults in the U.S.A. become septic each year. Furthermore, sepsis has also been diagnosed in 6% of hospitalized patients collectively^{1, 2}. N-terminal pro-Brain Natriuretic Peptide (NT-proBNP) is a cardiac-overload biomarker associated with cardiovascular disease and sepsis severity^{3,4}. It is an inactive fragment of the neuro hormone Brain Natriuretic Peptide (BNP). BNP and NT-proBNP are released into the bloodstream by cardiomyocytes in response to stress and pressure imposed on the atria and ventricles. However, their role in sepsis and septic shock is controversial. Growing evidence shows that NT-

proBNP may represent a useful prognostic biomarker in septic patients. In fact, it is noteworthy that elevated NT-proBNP has been associated with an almost seven-fold higher risk of mortality in sepsis^{5,6,7,8} and is a predictor of survival when compared to traditional biomarkers of sepsis including procalcitonin (PCT)^{9,10,11}. Recent studies have shown that the levels of BNP were increased in cases of sepsis or septic shock, regardless of the presence or absence of cardiac dysfunction.

ProBNP has also been found as a useful biomarker in predicting prognosis and length of hospital stay in some studies. Many have thus begun to explore the possibility of using BNP as

a predictor of morbidity, mortality, and hospital stay. Currently, there are various other scoring systems and biomarkers such as MEDS score, SOFA score, SAPS II, CRP, PCT and lactate. However, a few studies have shown that proBNP in comparison to MED score, SAPS II score and SOFA score was found equally good in predicting prognosis at 4 weeks as well as on length of hospital stay.

Some studies have shown that levels of BNP were significantly higher in non-survivors than in survivors. Others have shown that whereas there is no single biomarker that can accurately predict multiple organ dysfunction (MODS), selected biomarkers, among which is BNP, can be beneficial in predicting the outcome of patients in sepsis and septic shock^{12, 13, 14}

As per our knowledge, this type of study has not been done in the United Arab Emirates (U.A.E.) before.

This study was conducted to discover the prognostic significance in terms of length of hospital stay and proBNP in septic patients with no evidence of heart disease. Based on literature review, most studies could establish a relation between proBNP and mortality. In this study we aim to find a relation between proBNP and length of hospital stay. We believe such a study might give an insight into the outcome of septic patients and be a guide for further management plans, while establishing the role of proBNP in such patients.

MATERIALS AND METHOD:

Design of the Study:

ICD codes for patient with sepsis were determined from SALAMA EPIC electronic medical record system at Dubai Hospital. A list of patients was obtained from quality department of Dubai Hospital. A total of 123 patients were included in the sample after screening according to the inclusion and exclusion criteria. Due to incomplete records on the electronic medical system, only 48 patients could be included for analysis. Data was collected, entered on Microsoft Excel 2016 which was then analysed using SPSS version 26. For analysis levels of proBNP at admission, they were classified into normal (less than 125pg/mL), moderate (125pg/mL to 1000pg/mL) and high (more than 1000pg/mL). Procalcitonin levels were classified into mildly elevated (less than 0.25ug/mL), moderately elevated (0.25ug/mL to 0.49ug/mL) and markedly elevated (more than or equal to 0.50ug/mL). In this study we categorized outcome of patients into discharged or deceased. Amongst those who were discharged, length of hospital stay was further divided into less than or more than 3 days.

This research was approved by Dubai Scientific and Research Ethics Committee (DSREC).

Inclusion Criteria:

Both male and female patients admitted in High Dependency Unit (HDU) of Internal Medicine department of Dubai Hospital.

Duration from August 2017 until April 2019.

Age more than or equal to 14 years

All ethnicities.

Any patient with diagnosis of sepsis or septic shock with proBNP checked on admission.

Exclusion Criteria:

Patients in Intensive Care Unit (ICU)- Hemodynamically unstable or intubated

Patients below 14 years

Patient with history of acute coronary syndrome (ACS) or ST-T changes, rhythm disturbance on ECG.

Patients with following diagnoses:

- Clinical (raised jugular venous pressure, basal crepitation's in lungs and pedal edema) or echocardiographic evidence of heart failure (HFREF or HFPEF)
- Pulmonary embolism.
- Valvular heart disease.
- Infective endocarditis.
- Post CPR.
- Patients with pacemaker.
- Patients on invasive ventilation.

Descriptive and Statistical Analysis: Age, values of proBNP and Procalcitonin (PCT) were analysed through median and range whereas count and percentage was used to analyze gender, ethnicity, length of stay, outcome and categories of levels of PCT and proBNP. Cross tabulation using Fisher's exact score was then carried out between categories of proBNP level, categories of PCT level, ethnicity of patient with both categories of length of stay or outcome. A p-value of less than 0.05 was considered to be significant.

RESULTS:

A total of 48 patients' data was analysed in this study out of which 67% (n=32) were males while 33% (n=16) were female.

Median age of patients was found to be 72.5 years. Ethnic distribution showed 58% (n=28) of patients were from the Middle East and Africa (MENA) region, 35% (n=17) from Asia, 4% (n=2) from Europe and for the remaining 3% (n=1) ethnicity was not recorded.

In our study, 4.2% (n= 2) of the patients were found to have normal levels of Pro-BNP, while 16.7% (n= 8) were in the moderate and 79.2% (n=38) in the markedly high range.

25 % (n=12) of the patients were found to have mildly elevated levels of PCT, 17% (n=8) were found to have moderately elevated, and 58% (n=28) of the patients were found to have markedly elevated levels of PCT.

The percentage of patients discharged within 3 days (72 hours) was 6.3% (n=3) only, whereas 81.3% (n=39) were discharged after 3 days of hospitalization. 12.5% (n=6) of the patients deceased during their period of hospitalization.

This study was unable to establish a statistically significant relation between pro-BNP levels and length of stay (p= 0.279) as seen in Table 1. There was no statistically significant relation found between levels of PCT and length of stay (p = 1) as seen in Table 2. A statistically significant relation was found between ethnicity

and length of hospital stay with a p value of 0.04 as shown in Table 3.

Figure Legends:

		NLOS		Total
		LOS<3	LOS>3	
PRO-BNP (pg/ml) <125	Count	1	1	2
	% within PRO-BNP (pg/ml)	50.0%	50.0%	100.0%
>1000	Count	4	34	38
	% within PRO-BNP (pg/ml)	10.5%	89.5%	100.0%
126 to 1000	Count	1	7	8
	% within PRO-BNP (pg/ml)	12.5%	87.5%	100.0%
Total	Count	6	42	48
	% within PRO-BNP (pg/ml)	12.5%	87.5%	100.0%
P value – 0.279				

Table 1: Association between proBNP and Length of Stay (LOS) in days

		LOS<3	LOS>3	Total
PCT (ug/L) <0.25	Count	1	11	
	% within PCT (ug/L)	8.3%	91.7%	100.0%
>= 0.5	Count	4	24	28
	% within PCT (ug/L)	14.3%	85.7%	100.0%
0.25 to 0.49	Count	1	7	8
	% within PCT (ug/L)	12.5%	87.5%	100.0%
Total	Count	6	42	48
	% within PCT (ug/L)	12.5%	87.5%	100.0%
P value – 1.000				

Table 2: Association between levels of Procalcitonin and Length of Stay (LOS) in days

		NLOS		Total
		LOS<3	LOS>3	
ETHNICITY Asia	Count	2	15	17
	% within ETHNICITY	11.8%	88.2%	100.0%
Europe	Count	1	1	2
	% within ETHNICITY	50.0%	50.0%	100.0%
Middle east and Africa	Count	2	26	28
	% within ETHNICITY	7.1%	92.9%	100.0%
Unknown	Count	1	0	1
	% within ETHNICITY	100.0%	0.0%	100.0%
Total	Count	6	42	48
	% within ETHNICITY	12.5%	87.5%	100.0%
P value – 0.04				

Table 3: Association between Ethnicity and Length of Stay (LOS) in days

DISCUSSION:

Our study shows no significant relation between pro-BNP levels and length of stay as well as levels of PCT with length of stay. However, a statistically significant relation was found between ethnicity and length of hospital stay.

Majid Shojaee et al in 2018 conducted a cross sectional study on 121 patients from emergency department which compared proBNP and MEDS score. The study concluded that both predictors have high accuracy in predicting one month mortality of patients with sepsis but considered proBNP to be more convenient.¹⁵

Andrea Igoren et al studied 40 consecutive patients with severe sepsis where 55% of the patients had deceased at 4 weeks following hospitalization. This study further discovered that proBNP >1000 pg/ml at 72 hours was associated

with adverse outcome on the 28th day of hospitalization.¹⁶

Another study conducted by Alain Rudiger et.al in 2008 assessed the relationship between proBNP in 12 critically ill patients, half with acute heart failure and the other half with septic shock. The study found no significant difference in proBNP levels in both groups.¹⁷

Brigitte Meyer et al in 2007 also conducted a prospective observational study on 289 patients admitted to the intensive care unit and showed that non survivors had significantly high proBNP in comparison to survivors. He further concluded that proBNP on admission can be a prognostic marker of outcome and a single measurement.¹⁸

CONCLUSION:

This study did not show strong association between proBNP and prognosis in terms of length of hospital stay in septic patients in the absence of previous cardiac diseases.

LIMITATIONS:

This study was conducted in a retrospective manner. As per our hospital policy, no serial ProBNP levels are conducted. Hence, only those patients who had proBNP levels ordered on admission were included. Thus, the sample may not accurately represent the population of septic patients. Hence limiting the results.

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

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