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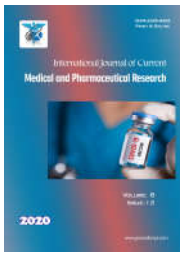

Research Article

ROLE OF D-DIMER AND BNP IN ENHANCING THE ABILITY OF qSOFA FOR EARLY IDENTIFICATION OF SEPSIS- A PROSPECTIVE OBSERVATIONAL STUDY IN THE EMERGENCY DEPARTMENT

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ABSTRACT

Introduction: The new definition has abandoned the use of host inflammatory response syndrome criteria (SIRS) in identification of sepsis and eliminated the term severe sepsis. As part of the 2016 SCCM/ESICM evaluation of criteria for identifying septic patients, the task force compared traditional SIRS criteria to other methods, including the Logistic Organ Dysfunction System (LODS) and Sequential Organ Failure Assessment (SOFA) scoring. One limitation of the new definition is the poor sensitivity of the qSOFA scoring system, which likely excludes its use as a screening tool for early sepsis, the stage in which treatment is most effective. We have evaluated the possibility of D dimer and BNP assays in addition to qSOFA score in early identification of sepsis.
Methodology: Using a POC triage meter, D dimers and BNP estimation were performed within one hour of arrival of possible septic patients.
Results: D dimers have significantly improved the performance of qSOFA in identifying true sepsis. (P 0.003)
Conclusion: D dimer estimation can add to early estimation of sepsis in the emergency department.

INTRODUCTION

Sepsis is the major diagnosis reaching our emergency department. It is a life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] Septic shock is a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality. Certain vital sign abnormalities notably fever, hypotension, and tachycardia are a hint to sepsis. Most important advancement in sepsis 3 guidelines is the introduction of qSOFA (Quick Sequential Organ Failure Assessment) score. It is a simple screening tool which includes altered mental status, respiratory rate ≥22 breaths/min, and systolic blood pressure ≤100 mm Hg . A score ≥2 helps to identify patients at higher risk of poor outcome. [2] However, there are many other conditions like polytrauma and some poisonings which can exhibit similar abnormalities in these three parameters .The history often can be inconspicuous which can further lead to confusion.

We have estimated the serum levels of D- dimers and BNP in all patients who have presented with history suspicious of sepsis with a positive qSOFA score.

The estimation was done at the time of first contact with the patient within the platinum hour of resuscitation. 2 ml venous blood was collected in EDTA vial and analysed using Abbott ® triage meter. The SOB panel reports 5 parameters namely d- dimer, BNP, CKMB, TropI and Myoglobin.The objectives of our study were to verify if **qSOFA** was good enough to predict sepsis for our patients and whether addition of **D**-dimer and BNP to qSOFA improves the prediction/classification of sepsis patients over and above that of qSOFA alone. The role of age and gender of patients were also studied as predicting poor outcome in sepsis. Sepsis was confirmed later with a positive blood culture. Rest cases were considered as No sepsis patients. The statistical analysis was performed on SPSS software ® version 24, Illinois, USA. Logistic regression was applied to compare the patient outcome with qSOFA,D dimer, BNP and all together for the best fit model. The ROC curves were constructed to calculate the accuracy of parameters in the classification/differentiation of sepsis from No-sepsis. The optimal cut off-values for predictors to differentiate sepsis from No-sepsis cases with values chosen with maximum sensitivity and highest possible accuracy was also computed statistically.

Results- A total of 158 patients were studied over a period of six months. 21 patients were diagnosed with sepsis and 137 patients were proven for no sepsis. Gender wise, 95 were males and only 63 were females. In age distribution, maximum number of patients enrolled for study were between the age of 57 to 70 years followed by 44 to 57 years of age. In our study, patients at extremes of age were less diagnosed with sepsis. The mean age (± SD) of patients with sepsis was

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58.70 (16.19) and was 56.06 (15.34) for No sepsis. All patients had qSOFA score ≥2 (100%), out of which 65 patients had a qSOFA score of 3. Table 1 summarizes the values of D dimers and BNP in study patients. D-dimers were increased in both groups as all patients were critically ill. However, the increase was twice as high in sepsis than in no sepsis group. BNP values were almost similar in patients with sepsis and no sepsis, but were higher than normal in all patients.

There are 20 patients with qSOFA score of 3 and only one patient with qSOFA score of 2 out of 21 patients who were diagnosed with sepsis with blood culture positive. There are 35 patients with SOFA score of 3 who are not diagnosed with sepsis it indicates that qSOFA is neither sensitive nor specific for diagnosis of sepsis.

Table 1 Summary statistics of study parameters

S. No	Measure	Sepsis Mean (SD) No. of patients(N)	No Sepsis Mean (SD) No. of patients(N)	Total no. of patients
1	D dimer	4648.57(671.61) N= 21	2111.39(1458.12) N=137	158
2	BNP	1455.86(1140.62) N= 21	1277.77(1369.16) N=137	158

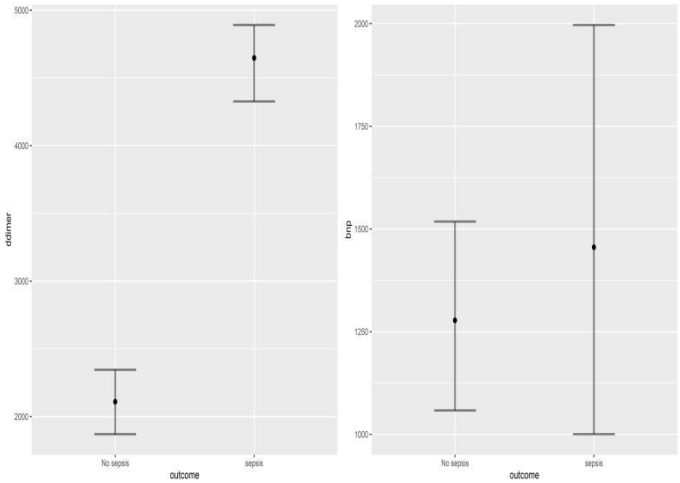

Figure 1 comparative analysis of study parameters in both groups with box plots.

The outcome i.e., a confirmed sepsis case was compared using ANOVA with parameters under investigation. Table 2 clearly demonstrates that addition of D- dimer estimation has significantly improved the recognition of true positive cases of sepsis. Additionally, age (p 0.711) and sex (p 0.412) were not helpful in improving the sepsis identification of qSOFA.

Table 2 comparative analysis of statistical performance of all 4 models

ANOVA	OUTCOME↔SOFA	OUTCOME↔SOFA+D DIMER	OUTCOME↔SOFA+BNP	OUTCOME↔SOFA+D DIMER +BNP
residuals	91.26	65.31	88.04	64.87
deviance	-	25.98	-22.73	23.17
P(> chi square)		3.438e-07***		1.477e-06***

ROC curve analysis (Figure 2) specified AUC of 0.812 for qSOFA and an AUC of 0.937 for a combination of qSOFA and D dimer. The comparative statistical significance (bootstrap) is 0.0000181.

ROC analysis from our study for predicting sepsis from the model 2, ie qSOFA with D dimer suggested following cutoff values for prediction of sepsis with 100% sensitivity and maximum possible accuracy of 77.22% are a qSOFA >2, D dimer ≥ 2350ng/ml.

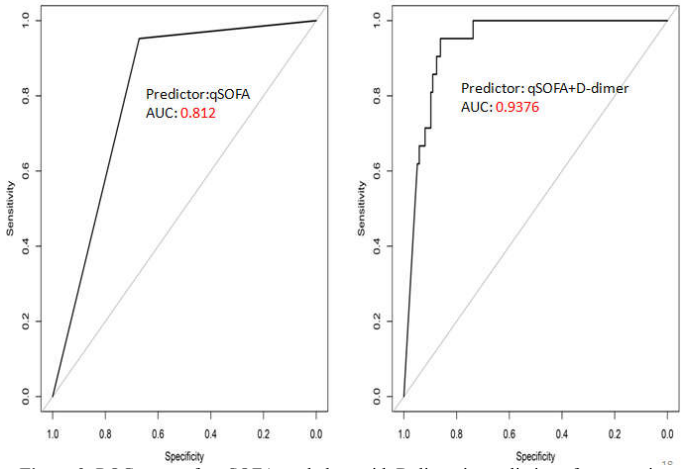

Figure 2 ROC curves for qSOFA and alongwith D dimer in prediction of true sepsis

DISCUSSION

The importance of early identification of sepsis is already described. This helps in immediate resuscitation and application of sepsis bundles, which is known to positively affect the patient outcome in terms of morbidity and mortality. multiple studies have discussed the questionable role of qSOFA in identifying sepsis. It seems that the score is more important for prognostication. The addition of certain biomarkers like lactates have already been researched extensively.

In 2010, Philip J Goebel *et al* studied the performance characteristics of D dimer in patients with presumed sepsis.[3] In septic patients endothelial activation may lead to locally induced coagulation. A large variety of fibrin compounds can be detected in plasma from patients with intravascular coagulation activation. D-dimer assays predominantly detect high molecular-weight cross linked fibrin complexes and there by D-dimer might be used as a marker of microcirculatory failure. The causal factors of elevated BNP levels in sepsis and septic shock are multifactorial. However, elevated BNP ranges (>230 pg/mL) were significantly associated with myocardial dysfunction and severity of global tissue hypoxia. The raised BNP is attributed to myocardial dysfunction and is characterized by ventricular stretch. Govind P *et al* has studied this biomarker extensively in prognostication, management and outcome of sepsis.[4]

CONCLUSION

D-dimer substantially adds to the ability of qSOFA In distinguishing sepsis from Non-sepsis patients. BNP is not a useful predictor of sepsis. Age and gender do not affect the ability of qSOFA& D-dimer in predicting sepsis

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