ORIGINAL ARTICLE

SHOCK INDEX AS A PREDICTOR OF HYPERLACTATEMIA FOR EARLY DETECTION OF SEVERE SEPSIS IN PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT OF A LOW TO MIDDLE INCOME COUNTRY

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Background: Early detection of sepsis in the emergency department is of prime importance and requires tools that are time and cost-effective. The Systemic Inflammatory Response Syndrome (SIRS) has been poorly associated with sepsis. Timothy *et al* in a retrospective analysis of Emergency Department (ED) visit stated estimate of SIRS at 17.8% accounting to an annual yield of 16.6 million adult visits with SIRS per year, among these only 26% accounted as an infectious aetiology of SIRS, trauma being 10% and other causes being rare. Shock index is found to be independently associated with 30-day mortality in a broad population of ED patients including sepsis. With limited health resources in a low to middle income country, focused utilization is important and so is the need for markers that are non-invasive, readily available, cost effective, and easy to interpret. Shock index can serve this purpose as a surrogate marker of disease severity in patients with severe sepsis and thus resulting in early detection of such patients. **Methods:** This cross-sectional study was conducted from December 2014 to May 2015 at a tertiary care setup (Aga Khan University Hospital) in Karachi consisting of all septic patients received at the emergency department. Non-probability sampling technique was used. p-value ≤ 0.05 was taken as significant. **Results:** Out of 180 study participants 94 (52.22%) were males while 86 (47.78%) were females. The mean age was 57.48±18.8 years. Cohen's κ was used to determine an agreement between the Shock index and Lactate levels. Shock index with cut off value of > 0.7 was used and moderate to the strong agreement between the two was found with kappa κ = 0.786 which was statistically significant (p=<0.001). Sensitivity was found to be 0.99, specificity 0.75, NPV 0.98, PPV 0.87. **Conclusion:** To conclude the shock index has some very favourable features, including availability, low cost, and direct relevance to sepsis in terms of its high validity. A high SI predicts elevated lactate levels in patients with sepsis.

Keywords: Sepsis; Severe sepsis; Septic shock; Lactate levels; Shock index

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INTRODUCTION

The epidemiology of Systemic Inflammatory Response Syndrome (SIRS) has been poorly understood. Timothy *et al* in a retrospective analysis of Emergency Department (ED) visits by adults published in 2014 stated an estimate of 372, 844 ED visits over four year period with an estimate of SIRS at 17.8% accounting to an annual yield of 16.6 million adult visits with SIRS per year, among this only 26 % accounted as an infectious aetiology of SIRS, trauma being 10% and other causes being rare.[1]

The term SIRS was coined to uncurtail a larger entity used to describe the physiological response to acute insults broadly classified as stated in the Tintinalli Textbook of Emergency Medicine as infectious (sepsis) and non-infectious (pancreatitis, trauma, ischemia, haemorrhage) respectively.[2]

Severe sepsis and septic shock being a sequel of sepsis constitute an immense healthcare burden affecting millions of people around the world each year killing one in four and increasing in incidence.[3]

The global prevalence of severe sepsis patients initially presenting with either hypotension with lactate ≥ 4 mmol//L, hypotension alone, or lactate ≥ 4 mmol/L alone, is reported as 16.6%, 49.5%, and 5.4%, respectively.[3]

Mortality rates increase linearly with severity at presentation, the mortality rates of SIRS, sepsis, and septic shock were 7, 16, and 46 percent, respectively.[4] Mortality appears to be lower in younger patients (<44 years) without comorbidities (<10 percent). Consensus guidelines recommend immediate diagnostic testing for adult patients with SIRS and a suspected infection.[5]

Patients with suspected or documented sepsis typically present with hypotension, tachycardia, fever, and leucocytosis. As severity worsens, signs of shock (for example cool skin and cyanosis) and organ dysfunction develop (for example oliguria, acute kidney injury, altered mental status).[6] Serum lactate is an entry criterion for early goal directed therapy protocol and is considered as an established marker of sepsis severity and hyperlactatemia (Serum Lactate ≥4 mmol/L) and has been used as an objective measure of disease severity and predictive of mortality as being a readily available marker for tissue hypoxia in patients with sepsis and severe sepsis.[7]

Systemic Inflammatory Response Syndrome criteria has been criticized for their limitation in identifying hyperlactatemia and has frequently been replaced by shock index (SI). The incidence of hyperlactatemia was 3 times higher in patients with SI ≥0.7 and in patients who met the SIRS criteria. The negative predictive values for a normal SI and the absence of SIRS criteria for identifying elevated lactate levels were both 0.95, and the sensitivities of SI ≥ 0.7 and of ≥ 2 SIRS criteria were not significantly different. The study concluded that a normal SI predicted the absence of increased lactate levels and that the SI would be useful in triage situations because of its immediate availability.[4]

In a study done by Rady *et al* SI ≥0.9 was predicted higher illness priority at triage, higher hospital admission rates, as well as intensive therapy on admission than pulse or blood pressure alone.[8]

Shock Index, first described by Allgower and Burri in 1967, is defined as heart rate divided by systolic blood pressure.[9] In healthy individuals the normal range of SI is from 0.5–0.7. SI is a simple and effective means of measuring the degree of hypovolemia in haemorrhagic and infectious shock conditions. Experimental and clinical studies have shown that SI is linearly inversely related to physiologic parameters, such as cardiac index, stroke volume, left ventricular stroke work, and mean arterial pressure.[8]

Shock index is found to be independently associated with 30-day mortality in a broad population of ED patients, and a shock index greater than or equal to 1 is associated with an adjusted OR of 10.5 (95% CI 9.3 to 11.7) for 30- day mortality.[8] Berger *et al* reported the agreement between Shock Index and Serum Lactate levels to be 83%.[7]

With limited health resources in a low to middle income country focused utilization of resources is important and so is the need for markers that are non-invasive, readily available, cost effective and easy to interpret. Shock index can serve this purpose as a surrogate marker of disease severity in patients with severe sepsis and thus resulting in early detection of such patients.

MATERIAL AND METHODS

This cross-sectional study was conducted from December 2014 to May 2015 at a tertiary care setup (Aga Khan University Hospital) in Karachi consisting of all septic patient received at the emergency department in the given time duration, Participants were selected through Non-probability sampling technique. SPSS 20 was used for data analysis. *p*-value <0.05 was taken as significant.

The sample size of 97 at 6.4% prevalence was calculated utilizing WHO sample size calculator for the standard formula of prevalence as[10]

$$n= z2\ p\ (1\text{-}p)/d2$$

The initial sample size of 90 showed data that was skewed due to many outliers so the sample size was inflated to 180 to accommodate non response, incomplete questionnaire, and to increase the power and reliability of results. The sample was selected through Non probability consecutive sampling technique.

All septic patients of age 16 years and up to 60 years of either gender who were being screened for Severe Sepsis with any infectious aetiology, i.e., in whom serum lactate level have been sent were included in the study while severe sepsis is defined as sepsis plus sepsis-induced tissue hypoperfusion (blood lactate concentration ≥4 mmol/L).[11] Exclusion criteria included patients on drugs affecting the heart rate, patients with permanent pace maker in place and patients with non-infectious aetiologies (e.g. Trauma, CVA, STEMI).

The patient who presents to ED-AKUH were triaged according to Emergency Severity Index-IV (ESI-IV), with an electronic patient's data base system. ESI is a five-level American triage scale developed by ED physicians Richard Wuerz and David Eitel in 1999–2000 to prioritize the patients and in addition to asking which patient should be seen first, triage nurses use the ESI to also consider what resources are necessary to move the patient to final disposition.[12] At the triage counter a standard set of vital signs were measured of all patients including blood pressure (BP), heart rate (HR), respiratory rate (RR), oral temperature, and Oxygen saturation via Pulse Oximetry.

All those patients who were being managed in ED with any infectious aetiology (as determined by on call ED Physician and mentioned on patient case file notes) were enrolled using electronic generated medical record numbers and were assessed for sepsis using a check list of a set of clinical signs, vitals and laboratory parameters. The only initial set of vitals done at triage or directly in the resuscitation area based on triage disposition and before any therapeutic intervention. These first vitals that were taken before any therapeutic intervention were used in each case to determine shock index. Patient fulfilling the criteria of Sepsis and in whom serum lactate was sent for screening of Severe Sepsis based on the clinical assessment of on call ED physician constituted the study subjects. This lactate level was sent along with other relevant investigations of these patient by the primary physician so no additional lab work up was done or requested for this study hence no consent was required. The result of the first available serum lactate level were taken for this study using the online software of patient care inquiry irrespective of the time when it was sent. Data for the vital sign and clinical variables were collected using case file notes while laboratory variables were collected using Patient Care Inquiry Software. Data was collected at the end of each month by retrieving the selected case files from Department of Health Information Management System (HIMS) and the case files were selected using the admitting or discharge diagnosis of Sepsis, Severe Sepsis and specific infectious aetiologies.

Blood Pressure and heart rate were 4mm measured by DATASCOPE PASSPORT 2 patient monitors, while the temperature is measured with mercury based oral thermometer. Serum lactate was measured with SIEMEN DIMENSION using serum immunoassay. As serum lactate levels is monitored in septic patients for the screening of severe sepsis as per surviving sepsis campaign guidelines so consent was not taken. During the process of data collection, clinical decision making and patient care were not affected.

Data was entered using SPSS version 20. Mean and standard deviation were used for numerical variables like age whereas frequency and percentages were used to represent categorical variables like gender, the major source of sepsis, patient disposition. The agreement was determined using kappa between the shock index and lactate levels. SI (shock index) with cut off value ≥0.7 were considered as positive, whereas Serum lactate levels of ≥4.0 mmol/L was regarded as hyperlactatemia, these cut-offs were used for identifying patients with severe sepsis as defined earlier, and agreement positive and agreement negative were determined for patients with severe sepsis. Different values of κ and their interpretation are shown in table-1. A contingency table was computed using chi-square between lactic acid and shock index to determine association. (Table-2) Sensitivity, specificity, Negative Predictive Value (NPV), Positive predictive value (PPV) were computed using standard formulas[13] for these specific variables, for this contingency table plotted between shock index (disease positive and negative) and lactate levels ≥4 mmol (test positive and negative). Hence as illustrated in table-3.

RESULTS

Out of 180 study participants, 94 (52.22%) were males while 86 (47.78%) were females. The mean age of the participant included in the study was 57.48±18.8 years.

The major source of sepsis identified among our study population was Respiratory system (47.2%) as pneumonia, followed by Genitourinary System (21.1%) and Urinary Tract Infection (10%).

Patient disposition consisted of n=154 (85.6%) being admitted as in-patient services out of these majority were offered admission in Special care Units (62.2%). Cohen's κ was run to determine if there exists an agreement between Shock index and Lactate levels in patients with severe sepsis. Shock index with cut off value of > 0.7 (SI) was used and moderate to a strong agreement between the two was found with kappa κ = 0.786 which was statistically significant (*p*=<0.001). Graph was plotted for performance of shock index for hyperlactatemia (LA ≥4.0 mmol/L). (Figure-1). The ability of shock index to predict need of admission was analysed in septic patients as well, to determine the level of care, the majority of the patient population had >0.7 on admission and were more likely to get admitted in Intensive care units as compared to those with shock index <0.7. We performed sensitivity, specificity, negative predictive value (NPV), Positive predictive value (PPV) for shock index of >0.7 performings for hyperlactatemia as defining the presence of severe sepsis (LA >4 mmol/L) and absence (LA <4 mmol/L). Using a 2 by 2 contingency table these values were calculated. (Table-2)

Sensitivity was found to be 0.99, specificity 0.75, NPV 0.98, PPV 0.87. (Table-3)

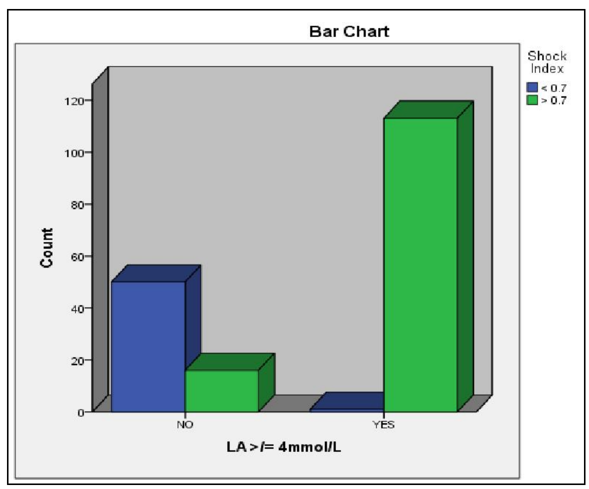

Figure-1: Performance of Shock Index (SI) for Hyperlactatemia (LA ≥ 4.0mmol/L)

Table-1: Interpretation of κ values

Value of Kappa	Level of agreement
0–0.20	None
0.21–0.39	Minimal
0.40–0.59	Weak
0.60–0.79	Moderate
0.80–0.90	Strong
Above 0.90	Almost Perfect

Table-2: Shock Index * LA >/= 4mmol/L Crosstabulation

			LA >/= 4mmol/L		Total
			NO	YES	
Shock Index	< 0.7	Count	50	1	51
		% within Shock Index	98.0%	2.0%	100.0%
		% within LA >/= 4mmol/L	75.8%	0.9%	28.3%
	> 0.7	Count	16	113	129
		% within Shock Index	12.4%	87.6%	100.0%
		% within LA >/= 4mmol/L	24.2%	99.1%	71.7%
Total		Count	66	114	180
		% within Shock Index	36.7%	63.3%	100.0%
		% within LA >/= 4mmol/L	100.0%	100.0%	100.0%

Table-3: A contingency table between shock index and lactic acid for validity of shock index

		Lactic acid	
		>4mmol	<4mmol
Shock index	>0.7	113[a]	16[b]
	<0.7	1[c]	50[d]
aTrue Positive	bFalse Positive	cFalse Negative	dTrue Negative

DISCUSSION

Measurement of serum lactate had long been known as a risk-stratification and predictor of in-hospital morbidity and mortality in identifying high-risk population in the emergency department. With this ever-evolving idea of early identification and treatment strategies for sepsis to uncurtail the growing needs and shrinking resources, fast and reliable screening tools are needed.[14]

Haas described, "The ideal triage tool as simple to use, accurate, rapid, reproducible and discriminative. The goal is to prevent potentially dangerous under-triage in the setting of high-acuity and high-uncertainty as witnessed in the emergency setting so as to prioritize sicker apparently well looking patients.[15]

Shock index (SI=Heart rate/Systolic blood pressure)[8] emphasizes this physiologic need as a reliable bed side screening tool for triaging patients. As screening for sepsis and the doom of fear associated with it being missed, demands the need to send laboratory specimens like serum lactate and apply SIRS criteria[16] as early from triage to save time, though, this has brought in the dilemma of false positives and abnormal test results that are followed by costly, time consuming and lengthy remediation process. Literature suggests that the patients with normal SI (less than 0.7) are 95% less likely to present with higher levels of established sepsis severity marker like serum lactate therefore normal SI may serve as a surrogate to SIRS criteria and prioritize patients for care in need of lactate levels so as to establish sepsis or its follow-through.[7] This was similar to our results where patients who were admitted with SI >0.7 were more likely to get inpatient intensive care unit admission and had a critical course in comparison to patients with SI of <0.7.[1]

Wira *et al*[17] studied a modification of the SI and measured it throughout the entire ED visit to determine if a sustained SI for longer periods was a better predictor of deterioration and the requirement for vasopressors in patients with severe sepsis. The 295 patients from the study came from an ED sepsis registry maintained over a 2-year period. For each set of vital signs taken on each patient, the SI was calculated until the patient required vasopressors. If the SI was greater than 0.8 on at least 80% of the measurements, the patient would be considered to have a sustained SI elevation. The patients with sepsis and sustained SI had lower initial blood pressures and higher heart rates. They had more organ dysfunction at presentation and tended to require more vasopressor use over the next 72 hours. As a result of this study, Wira *et al*[17] suggested that the sustained SI may be more useful than a single SI measurement as a predictor of the clinical course in the ED, the trend was similar to our study observation.

Strehlow MC *et al* in the National Hospital Ambulatory Medical Care Survey studied the frequency and disposition of adult ED patients with sepsis and has reported a greater number of female presentation when considering gender predisposition this is contrary to our findings, furthermore, Strehlow MC and his colleagues demonstrated larger number elderly patients aged +80 years whereas ours was a rather younger group with mean age of 57 years.[18]

Literature review suggests Urinary Tract infection to be the highest occurring culprit to sequel of sepsis whereas our population was victimized by respiratory tract involvement, pneumonia being the most common source of sepsis; though for Malayan population considering Asian origin trends remained the same as ours.[9]

Sixty-three percent of our population should a relationship having high lactate levels and were simultaneously positive for shock index, these were true positives, as evident by the literature review this was much higher in our side of the world which makes it an immensely valuable low cost bedside triage tool in our low to middle income society, which would forbidden the extra burden of cost sending sepsis panel of laboratory on low risk population.[19]

The validity of shock index is elucidated by sensitivity and specificity.[13] Sensitivity of shock index in our population in its true meaning as correctly identifying an individual as diseased was 99% which makes it a very efficient validated tool for screening patients with sepsis, also in regards to ruling out the disease, its specificity was 75% which increases the reliability of this test in preventing burden over with overtreatment or extensive workup. As this is a new concept emerging it has a reliable comparison to the current guidelines of using lactate levels as so by predicting true positives by 87%. Finally, its effectual state of estimating true negatives was 98% which was greater than as observed by Tony Berger *et al*[7] in their retrospective cohort.

CONCLUSION

To conclude shock index has some very favourable features, including availability, low cost, and direct relevance to sepsis in terms of its high validity. A high SI predicts elevated lactate levels in patients with sepsis.

AUTHORS' CONTRIBUTION

SW: Conception and design of the work. NA: Analysis and interpretation of data. SS: Data Collection and Manuscript writing. ES: Critical analysis of draft and final approval.

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