A Study on Shock Index in Early Diagnosis of Sepsis in Emergency Department of Tertiary Care Centre of Nepal

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ABSTRACT

Introduction: Sepsis and its consequences, severe sepsis and septic shock is at menace in country like ours where infectious disease are at toll. Early diagnosis and treatment is very important to decrease the morbidity and mortality. Shock index is one of such tool that is very handy in these situations as this is just a mathematical calculation using heart rate(HR) and systolic blood pressure(SBP). The main aim of this study is to find the effectiveness of using SI as an adjunct to blood lactate in diagnosing patients in sepsis.

Methods: This was an observational hospital based study conducted at Emergency Department of TUTH, Maharajgunj from 21stjuly 2016 to 13th October 2016, on 104 patients, obtained by purposive sampling method, who had presented to the "Red Area", aged between 18 to 65 years, who had presented with suspected infection. These patients were screened for severe sepsis u using triage vital signs, basic laboratory tests and an initial serum lactate level. Test characteristics were calculated for hyperlactatemia. I considered the following covariates in my analysis: heart rate >90 beats/min; mean arterial pressure <65 mmHg; respiratory rate > 20 breaths/min; ≥2 SIRS including white blood cell count; SI <0.6; SI 0.6 to 1; SI 1 to 1.4and SI ≥ 1.4. We report sensitivities, specificities, and positive and negative predictive values for the primary outcome.

Results: There was apositive correlation between shock index and blood lactate level, r=0.2, n=104, p=0.042.A chi-square test was performed and no relationship was found between SI>=1 and hyperlactemia, X2 (.285, N = 104) = 1, p =.594 and relationship was found between SI >=0.7 and hyperlactemia, X2 (4.1, N = 104) = 1, p =.04. sensitivity and specificity for detecting hyperlactemia of SI>=1, SI.=0.7, SIRS was 84% and 20%, 93% and 0%, 79% and 20% respectively. Negative predictive value of SI>=1, SI.=0.7 and SIRS was 63%, 0% and 57% respectively.

Conclusions: There was weak correlation between the lactate level and shock index with statistically significant correlation between the shock index grouped >=0.7 and hyperlactatemia with high sensitivity and very low specificity.

Keywords: *early diagnosis; sepsis; emergency.*

INTRODUCTION

Sepsis and septic shock is a progressive injurious process resulting from systemic inflammatory response to infection. It is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation). Early recognition and prompt resuscitation during the first several hours of severe sepsis and septic shock helps to optimize outcome.

The main aim of this study is to find the effectiveness of using SI as an adjunct to blood lactate in diagnosing patients in sepsis.

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METHODS

This was an observational hospital-based study conducted at Emergency Department of TUTH, Maharajgunj from 21st july 2016 to 13th October 2016, on 104 patients, who had presented to the "Red Area", aged between 18 to 65 years, obtained by purposive sampling, who had presented with suspected infection. Total patients that had visited the area were 1443 of which 275 were of suspected infection. Depending upon age group, 148 were screened. 104 patients were included in the study excluding incomplete records and referral from other hospital with initial resuscitation.

Inclusion criteria

1. Age group between 18 and 65
2. Patients in SIRS
   - Two or more of: Temperature >38˚C or <36˚C, Heart rate >90/min, Respiratory rate >20/min
   - White blood cell count >12 000/mm^3 or <4000/mm_3
3. Patients in Sepsis: SIRS with documented or suspected source of infection
4. Patients in Severe Sepsis
   - Any of the following thought due to the infection:

     Sepsis induced hypotension

     Lactate above upper limit of laboratory normal

     Urine output< 0.5 ml/kg/hr for more than 2 hrs despite adequate fluid resuscitation

     Acute lung injury with Pao2/Fio2 <250 in absence of pneumonia or Pao2/Fio2<200 in presence of pneumonia

     Creatinine> 176.8 umol/l

     Bilirubin> 34.2umol/l

     Platelet count < 100000/mm^3

     Coagulopathy (inr>1.5)

Exclusion criteria

1. Referred case from other hospital with initial resuscitation
2. Post cardio pulmonary resuscitation
3. Cardiogenic shock
4. Hypovolemic shock
5. Obstructive shock
6. Neurogenic shock

Lab investigations: As mentioned above in the the procedure following investigations were performed with cut off values used and evaluated for organ dysfunction.

1. Complete Blood Count(CBC)

   Total count = 4000-12000/mm_3

   Platelets= 100000/mm_3
2. International Normalization Ration (INR): =1.5
3. Renal Function Test (RFT)
   Creatinine: = 176.8 umol/l
4. Liver Function Test(LFT): bilirubin = 2 mg/dl (34.2umol/l)
5. Arterial Blood Gas Analysis(ABG)
   Lactate= 2.5mmol/l

Procedure: All the patients who had been triaged to the red area were evaluated and resuscitation started immediately without any delay. These patients were screened for severe sepsis using history of any suspected infection and triage vital signs. Venous blood samples were taken for hematology, biochemistry and blood cultures. Arterial blood was drawn from either radial or femoral artery in a heparinized syringe and an initial serum lactate level obtained via ABG. Test characteristics were calculated for hyperlactateemia (primary outcome) as a objective surrogate of severity and >2 OD (secondary outcome).

Later, following covariates were considered in my analysis: heart rate >90 beats/min; mean arterial pressure < 65 mmHg; respiratory rate > 20 breaths/min; ≥2 SIRS including white blood cell count; SI >=0.7; SI>=1. Sensitivities, specificities, and positive and negative predictive

values for the primary and secondary outcome was calculated.

Analysis: For ease of interpretation, the variables of interest (SI, SIRS, hyperlactatemia and >=2 organ dysfunctions) were categorized into categorical variables. Hyperlactemia was the primary outcome of interest as as a marker of severe sepsis. 3 distinct predictors of hyperlactemia and also organ dysfunctions were analyzed. Bivariate correlation between shock index and lactate level was done. Chi squared was used to analyze correlation between individually grouped shock index with grouped lactate level i.e. lactate >=2 and Lactate <2. Chi squared test to measure the statistical difference between proportions. Sensitivity, specificity, positive predictive value and negative predictive values for each of the four were measured. All calculations were performed using IBM SPSS statistics 23 and MS EXCEL for mac version 15.17.

RESULTS

Demographics and predictors dependent on cohort of lactate level

Table 1. Demographics and predictors of the full cohort stratified by hyperlactemia.

	Lactate >2.5mmol/l	Lactate <2.5mmol/l	P value	95% C.I.
Demographics				
Male	40.9% (18)	41.7% (25)	0.9	-18.5 to 21
Age	44.09±15.68	40.38±15.09	0.2	-2.26 to 9.678
Address				
KTM	38.6% (17)	28.3% (17)	0.2	-9.078 to 29.53
Duration of illness	5.3±3	7.27±5.36	0.034	0.1905 to 3.7495
Vitals				
Temperature	38.1±1.2	37.9±1.3	0.34	-0.2 to 0.7
Heart rate	108.7±18.085	105±16.9	0.3	-3.07 to 10.4
Respiratory rate	30.2±5.7	29.3±10.2	0.6	-2.4 to 4.263
Systolic B.P.	77.3±5.5	87±19.0	.001	-15.5 to -3.910
Diastolic B.P.	47.86±22.1	54.10±18.405	0.12	-14.04 to 1.56
MAP	56.9±22.7	63.2±19.0	0.094	-14.9 to 1.098
SIRS	79.5% (35)	80% (48)	0.9	-15.801 to 17.98
Laboratory investigations				
Total Count (/mm^3)	13112.1±7721.3	13551±9350.1	0.8	-3823.6 to 2945.7
neutrophils	78.8±11.1	78.5±13.6	0.9	-4.6 to 5.2
Platelets(/ mm^3)	109365.9±95538.2	144931±126940.5	0.1	-80205 to 9075.8
Prothrombin Time(PT)	18.7±5.1	17.37±13.86	0.5	-2.923 to 5.583
Billirubin (umol/l)	46.3±37.84	30.98±26.3	0.017	2.9 to 27.7
Creatinine (umol/l)	238±137.0	133±85.58	.0001	62.1 to 147.8
PO_2/FiO_2	299±79.1	340±88.9	.017	-74.0 to -7.9
Organ dysfunction	2.16±1.4	2.05±1.38	0.673	-0.4 to 0.6

Sirs, systemic inflammatory response syndrome. Continuous data expressed as the mean and standard deviation; categorical data expressed as percentage. Organ dysfunction >=2 organ dysfunction.

Relation between lactate level and shock index in patients with sepsis.

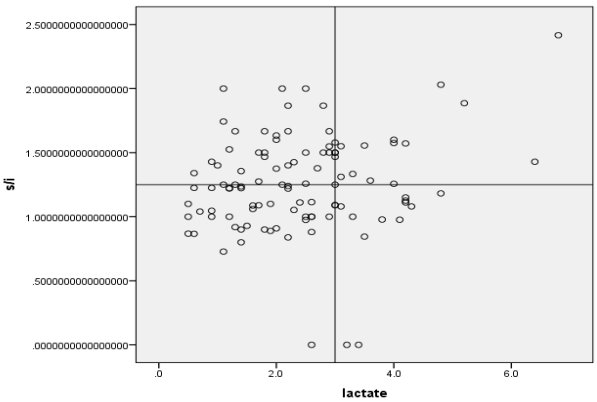

Figure 1. scatter dot between lactate level and shock index(SI)

Table 2. Pearson bivariate correlation. Positive correlation between the two variables,

Correlations

		s/i	lactate
s/i	Pearson Correlation	1	.200*
	Sig. (2-tailed)		.042
	N	104	104
lactate	Pearson Correlation	.200*	1
	Sig. (2-tailed)	.042	
	N	104	104

*. Correlation is significant at the 0.05 level (2-tailed).

r=0.2, n=104, p=0.042.

Table 3. chi squared test between lactate grouped and SI>=0.7

si0.7 * lactate grouped Crosstabulation

			lactate grouped		Total
			>2.5	<2.5	
si0.7	>=0.7	Count	41	60	101
		% within si0.7	40.6%	59.4%	100.0%
		% within lactate grouped	93.2%	100.0%	97.1%
		% of Total	39.4%	57.7%	97.1%
	<0.7	Count	3	0	3
		% within si0.7	100.0%	0.0%	100.0%
		% within lactate grouped	6.8%	0.0%	2.9%
		% of Total	2.9%	0.0%	2.9%
Total		Count	44	60	104
		% within si0.7	42.3%	57.7%	100.0%
		% within lactate grouped	100.0%	100.0%	100.0%
		% of Total	42.3%	57.7%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.212[a]	1	.040		
Continuity Correction[b]	2.130	1	.144		
Likelihood Ratio	5.283	1	.022		
Fisher's Exact Test				.073	.073
Linear-by-Linear Association	4.172	1	.041		
N of Valid Cases	104				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.27.

b. Computed only for a 2x2 table

Table 4. chi squared test between lactate grouped and si>=1

lactate*si >=1

			si1		Total
			1	<1	
lactate grouped	>2.5	Count	37	7	44
		% within lactate grouped	84.1%	15.9%	100.0%
		% within si1	43.5%	36.8%	42.3%
		% of Total	35.6%	6.7%	42.3%
	<2.5	Count	48	12	60
		% within lactate grouped	80.0%	20.0%	100.0%
		% within si1	56.5%	63.2%	57.7%
		% of Total	46.2%	11.5%	57.7%
Total		Count	85	19	104
		% within lactate grouped	81.7%	18.3%	100.0%
		% within si1	100.0%	100.0%	100.0%
		% of Total	81.7%	18.3%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.285[a]	1	.594		
Continuity Correction[b]	.076	1	.782		
Likelihood Ratio	.288	1	.592		
Fisher's Exact Test				.798	.394
Linear-by-Linear Association	.282	1	.596		
N of Valid Cases	104				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 8.04.

b. Computed only for a 2x2 table

Predictors of hyperlactemia and organ dysfunctions

Table 5. Performance of predictors of hyperlactemia.SI, shock index, SIRS, systemic inflamatory response syndrome, hyperlactemia, >2.5mmol/l

	SI>=1	SI>=0.7	SIRS
Positive predictive value	0.43	0.4	0.42
Negative predictive value	0.63	0	0.57
sensitivity	0.84	0.93	0.79
specificity	0.20	0	0.20

Table 6. Performance of predictors of organ dysfunction. SI, Shock Index, SIRS, Systemic Inflammatory Response Syndrome, hyperlactemia= >=2.5 mmol/l

	SI>=1	SI>=0.6	SIRS
Positive predictive value	0.64	0.62	0.63
Negative predictive value	0.46	0	0.38
sensitivity	0.89	0.95	0.8
specificity	0.15	0	0.20

DISCUSSION

Most screening tools depend on the identification of criteria used to define the systemic inflammatory response syndrome (SIRS). Management tools include serial measurements of blood pressure, heart rate (HR) and lactate levels, tracking organ dysfunction and invasive monitoring. The incidence of sepsis and sepsis-related mortality is reportedly lower in women, and several hypotheses have been proposed to explain this finding, including the role of sex hormones and sex-related gene polymorphisms associated with immune function.[1] In my study the male population (41.3%) was less than the female population (58.7%) in total cohort and was not comparable to the study by Glickman et al.1 and contradicting the theory. Bernato et al[2] has shown that incidence increases with age which holds true in our study too but in contrary, there is female predominance in the older age group.

The Drug Act of Nepal, implemented in 1978, classifies medicines into several categories and outlines regulation of their use. According to the act, antibiotics may be dispensed by drug sellers only upon receipt of a valid prescription.[3] In this study 25% of the total cohort had not taken any antibiotics. Of 75% of total population had taken antibiotics in one form or the other. There was statistical significance between the population taking antibiotics and not taking antibiotics.This shows that the most of the patients coming to the E.D. would have already consumed some antibiotics in the course of their disease one way or the other.

The most common source of infection was respiratory system (44 out of 104) and the gastrointestinal (19 out of 104) and the genitourinary system (15 out of 104) in order. As compared to the Glickman et al1 where pulmonary system (34%)was the most common one to be affected, and then the genitourinary(14%) and then gastrointestinal system(10%).

The sensitivity of SI >= 1 is 84% and specificity of 20%; the sensitivity of shock index >=0.7 was 93% but specificity of 0%; SIRS criteria had specificity of 79% with specificity of 20%. The incidence of organ dysfunction of >=2 was 64%, 62% and 63% respectively in SI group of >=1 and >=0.6 and SIRS. There was not much of difference in all these three populations. The negative predictive value (NPV) for SI >=1 was 63% i.e there is 63 % chance of patients with shock index <1 to detect hyperlactatemia. But if we see the same for SI <0.7 i.e. normal SI there is 0% chance of pts in normal shock index to present with normal lactate level. For negative predictive value for SIRS criteria >=2 was 79%, i.e there is 79% chance that there is no hyperlactatemia when the sirs criteria is <2 in pts with suspected infection. These results weren't comparable to the one done by Berger et al.[4] where 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. Since many factors affect abnormal vital signs, sensitivity and positive predictive values will vary the true reliability of the findings lies in the negative predictive values of the shock index. In this study shock index less than 1 has more negative predictive value (79%) predictive than shock index less than 0.7 with negative predictive value of 0%. Normal shock index has shown to most cost effective tool to predict and help clinician to prioritize for care.[5] But my study shows that there might be need of categorizing new cut off values for the shock index and further evaluation. The incidence of >=2 organ dysfunction was 64%, 62% and 63% in SI=1, SI.=0.7 and SIRS >=2 respectively. There is not much of difference in the incidence of hyperlactatemia in all these three groups. The negative predictive value of SI>=0.7 was 0%

similar to in prediction of hyperlactatemia. It had high sensitivity (95%) but with low specificity (0%) to predict organ dysfunction. There was no significant difference between the sensitivity of SI>=1 (89%) and SI.=0.7 (95%) p value of 0.3. the sensitivity was 80% of SIRS criteria >=2. The negative predictive value for all three predictors were low; SI>=1 40%, SI>=0.7 0% and SIRS >=2 38%.

Recently new guidelines have come up for screening of sepsis and severe sepsis. Sepsis 3 guidelines have come up with changes in the definitions of sepsis and septic shock with new tools for diagnosis and screening. In out-of-hospital, emergency department, or general hospital ward settings, adult patients with suspected infection can be rapidly identified as being more likely to have poor outcomes typical of sepsis if they have at least 2 of the following clinical criteria that together constitute new bedside clinical score termed quickSOFA (qSOFA): respiratory rate of 22/min or greater, altered mentation, or systolic blood pressure of 100mmHg or less. Even though it only uses clinical examination findings, but still needs prospective validation to confirm its robustness. Lactate measurement, important biochemical identifier of sepsis and also predictor of severity, was not considered in the sepsis 3 guidelines for the screening. This guideline has considered SIRS non-specific and now it is no longer used for sepsis recognition/screening.

CONCLUSIONS

There was weak correlation between the lactate level and shock index with statistically significant correlation between the shock index grouped >=0.7 and hyperlactatemia with high sensitivity and very low specificity.

CONFLICT OF INTEREST: None

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