Clinical Presentation of elderly patients with Sepsis with serial monitoring of HDL cholesterol levels as a prognostic marker

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Abstract
Background:*Sepsis is defined as a 'life-threatening organ damage as a result of dysregulated host immune response" (**Singer, M., et al 2016**) represented by increasing of patients'sequential organ failure assessment score by 2points or more. According to CDC approximately 1.7 million adults develop Sepsis each year leading to 2.7 lac deaths annually. Globally it is estimated 31.5 million sepsis and 19.4 million cases of severe sepsis with 5.3 million deaths annually. Sepsis is a very serious illness but can be particularly devastating for the elderly aged > 65years and is 13 times more likely to be hospitalized compared to adults < 60years. Sepsis and septic shock can result from infection anywhere in the body such as pneumonia, influenza or UTI.As per report on the medical certification of death 2015 based on Indian census report of 2011 a total of 11,83,052 medically certified deaths were cause of sepsis and septic shock with 30% male and 26% of ICU admission.****Methods:****This is an Observational Study conducted in Tertiary care Hospital in Assam for a period of 6 months which included a total of 60 patients (35male and 25female). Detailed clinical history, physical examination and laboratory investigations were performed in each case that were included in our study.Sepsis cases were screened at bedside with the help of qSOFA. **STATISTICAL ANALYSIS:** Statistical Analysis was carried out using Epi Info version 7.2.5.0 (CDC, US) software with Regression Modules installed, Microsoft installed, Microsoft word and Excel have been used to generate graphs, tablets etc.****Results:****A total of 60 patients were taken up for study, 35 were male patients and 25 were female patients, above 60 years of age who were hospitalized with evidence of sepsis and septic shock.Mortality was high (67%) and was associated with comorbidities and multi organ failure.Out of 60, only 20 patients (31.6%) recovered and were discharged from a hospital (DOS). Mean age in survivors were 68.8 whereas it was 72.7 in non survivors.The most common symptoms were fever (83.3%), tachycardia (71.6%) and tachypnea (78.3%).The HDL value of the survivors rose from 33.05 (day1) to 45.65 on day5, whereas in the non-survivors it dropped from mean of 34.9 to 23.83 from day of admission to day 5 and it wasstatistically significant. This shows that HDL valuedrops when sepsis is increasing and is lower in non-survivors in relation with survivors.****Conclusion:****There is a definite correlation of HDL levels with clinical outcome of patients with sepsis. Rising trend of HDL levels favoured improvement in clinical condition and better outcome while decreasing HDL levels implied worsening condition.Hence HDL levels can be used as a prognostic marker in sepsis. Thus, knowledge of HDL levels of patients with sepsis can be applied to give life-saving interventions and prevent multi-organ dysfunction.*
Key words: *Sepsis, qSOFA, HDL(High Density Lipoprotein).*

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I.   Introduction

Sepsis is defined as a 'life-threatening organ damage as a result of dysregulated host immune response" **(Singer, M., et al 2016)** represented by increasing of patients'sequential organ failure assessment score by 2points or more. According to CDC approximately 1.7 million adults develop Sepsis each year leading to 2.7 lac deaths annually. Globally it is estimated 31.5 million sepsis and 19.4 million cases of severe sepsis with 5.3 million deaths annually. Sepsis is a very serious illness but can be particularly devastating for the elderly aged > 65years and is 13 times more likely to be hospitalized compared to adults < 60years. Sepsis and septic shock can result from infection anywhere in the body such as pneumonia, influenza or UTI.

As per report on the medical certification of death 2015 based on Indian census report of 2011 a total of 11,83,052 medically certified deaths were cause of sepsis and septic shock with 30% male and 26% of ICU admission.

Aims and Objectives
- Clinical presentation of elderly patients with sepsis
- Serial monitoring of HDL-cholesterol levels as a prognostic marker

II. Review Of Literature

HDL-c LEVEL at the time of emergency department admission in septic patients was more predictive of Multiorgan dysfunction syndrome and 28day mortality (In another study of 64 patients with severe sepsis, no patient with an HDL-c >25mg/dl on day 3 died and the non survivors had persistently declining HDL levels). HDL-c undergoes qualitative changes which may contribute to multiorgan dysfunction and mortality.

Patients undergo many distinct changes in their lipid profile during acute physiological stress. Also, lipid mediators play a distinct role in innate immune signalling. HDL-C is a complex biological molecule consisting mainly of two proteins known as Apo-A1 and Apo-A2 surrounded by a lipid core. HDL-C has a myriad of biological function during inflammation.

Functional high-density lipoprotein (HDL) exhibits pleiotropic effects during an acute stress response:
1) supports endogenous corticosteroid stress-response.
2) Decreases platelet aggregation
3) Binds and clears bacterial toxins
4) Inhibits endothelial cell apoptosis
5) Reduces the monocyte inflammatory response
6) Inhibits expression of endothelial cell adhesion molecules like (VCAM)-Vascular cellular adhesion molecule/ (ICAM)- Intercellular cellular adhesion molecule/ e-Selectin

Comorbid conditions like diabetes, hypertension, immunosuppression, malignancy are associated with increased mortality and morbidity in patients with sepsis. In Diabetes patients there is alteration of immune function which is associated with recurrent, nosocomial and secondary infections leading to sepsis. Illness that depresses the defense mechanism of host to an invading pathogen can result in increased infections resulting in sepsis and septic shock. Patients with renal failure, hepatic failure, neoplasms, immunosuppressant therapy and steroid use are at increased risk of sepsis and death.

Though HDL is thought to be protective against sepsis it has been shown that when subjected to stress and acute inflammation HDL-c becomes prooxidant and proinflammatory.

III. Materials and Methods

This is an Observational Study conducted in Tertiary care Hospital in Assam for a period of 6months which included a total of 60 patients (35male and 25female). Detailed clinical history, physical examination and laboratory investigations were performed in each case that were included in our study

Sepsis cases were screened at bedside with the help of qSOFA which includes
i) Respiratory rate > 22/min
ii) Altered mental status (GCS<13)
iii) Systolic Blood Pressure $\leq$ 100 mmHg

The qSOFA score is a modified version of SOFA scoring for the assessment of sepsis at bedside. If 2 out of 3 parameter is positive at bedside patient is likely to have suspicion of sepsis.
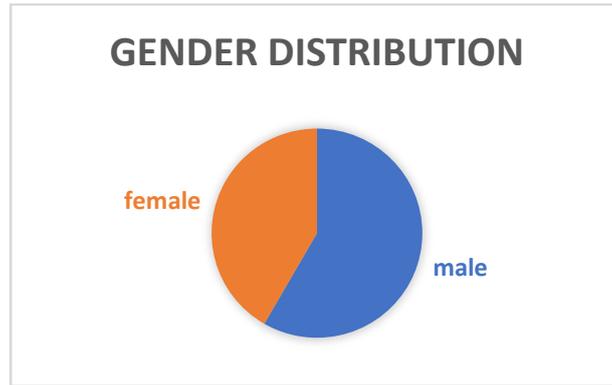
ETHICAL CLEARANCE: Ethical clearance was obtained from the Ethical Clearance Committee of tertiary care Hospital.

STATISTICAL ANALYSIS: Statistical Analysis was carried out using Epi Info version 7.2.5.0 (CDC, US) software with Regression Modules installed, Microsoft installed, Microsoft word and Excel have been used to generate graphs, tablets etc.

Results on continuous measurements are presented on Mean &SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance.

IV. Results and Observations

We included a total of 60 patients, 35 were male patients and 25 were female patients above 60 years of age who were hospitalized with evidence of sepsis and septic shock.

GENDER DISTRIBUTION

female   male

Mortality was high (67%) and was associated with comorbidities and multi organ failure.
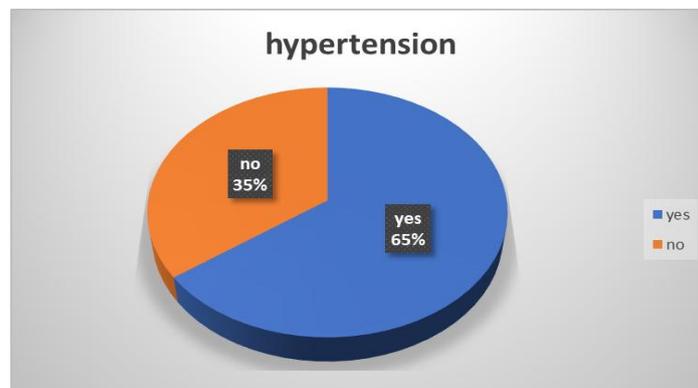
SURVIVAL

survivors
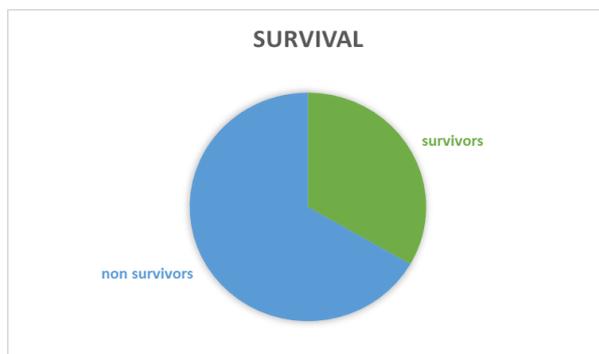
non survivors

Out of 60 patients, only 20 patients (33.3%) survived.

Out of 60, only 20 patients (31.6%) recovered and were discharged from a hospital (DOS). Mean age in survivors were 68.8 whereas it was 72.7 in non survivors.

mean age

Age

74
72
70
68
66

yes   no

■ mean
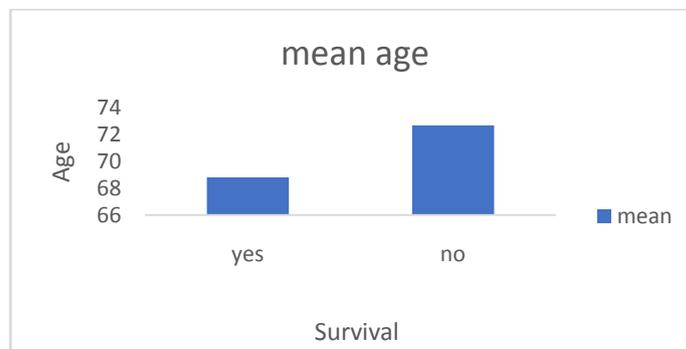
Survival

Out of 60, 39 cases were hypertensive (65%).

hypertension

no
35%

yes
65%

■ yes
■ no

The most common symptoms were fever (83.3%), tachycardia (71.6%) and tachypnea (78.3%).
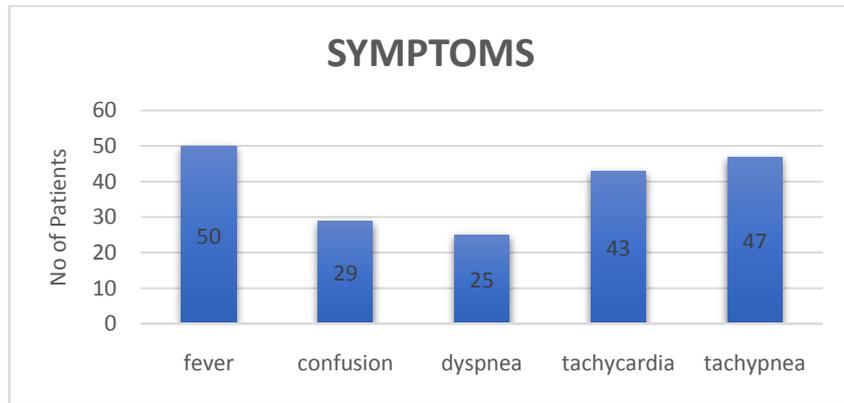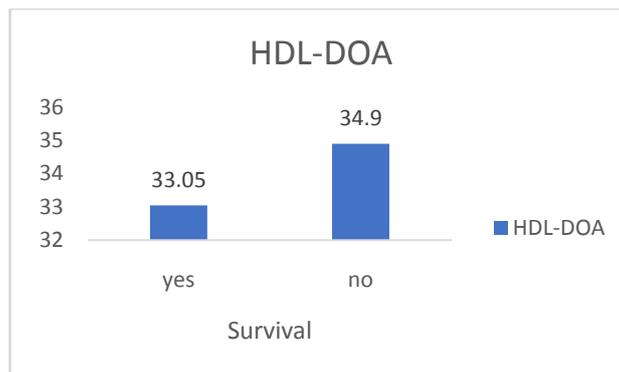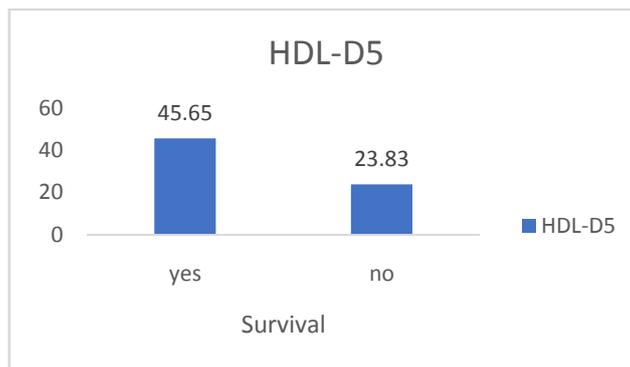

In the survivor group average duration of stay was 8.1 days whereas that in the non-survivors were 10.93.

HDL Cholesterol values with respect to Survival

Parameter	Survival				p-value
	Yes	SD	No	SD	
HDL-DOA	33.05	14.43	34.9	8.1	<0.05
HDL-D5	45.65	11.50	23.83	8.16	

The HDL value of the survivors rose from 33.05 (day1) to 45.65 on day5, whereas in the non-survivors it dropped from mean of 34.9 to 23.83 from day of admission to day 5 and it wasstatistically significant. This shows that HDL valuedrops when sepsis is increasing and is lower in non-survivors in relation with survivors.

V. Discussions

Sepsis is one of the leading causes of mortality worldwide. In spite of the availability of biomarkers for sepsis and mortality scores, the mortality for sepsis still has not decreased significantly. So, there is a need for development of more sensitive biomarkers for early detection of sepsis

From our study, it can be concluded that among the 60 patients, 35 were male and 25 were female and the survival rate was 33.3%%. In a similar study done by Sunayana,P., et al 2017 among 70 patients, 42 were male and 28 were female and survival rate was 72.8%. In a study of 111 patients conducted by Naresh,M., et al 2015, 67(60.4%) were males and 44(39.6%) were female with survival rate of 54%.

It is observed that among the non survivors, 77.50% were hypertensive patients when compared to survivors (50%), which implies that chronic medical conditions like that of hypertension play a significant role in survival in sepsis. In longitudinal cohort study using the 30,239 community-dwelling participants of the REGARDS cohort [(Reasons for Geographic And Racial Differences in Stroke (REGARDS)] by Wang,H.E.,et al 2006 there were 975 incident cases of sepsis, where they showed that incident sepsis episodes were associated significantly with chronic medical conditions like that of hypertension 1.49%.

From our study, it is observed that the most common presentation was fever (83.33%),followed by tachypnea(78.33%) and tachycardia (71.67%).

The duration for stay was assessed to measure the morbidity and was found to be prolonged in cases of expired patients with a mean duration of stay of 10.93 days when compared to patients who survived,with a mean duration of 8.1 days, and it was statistically significant.

HDL values were measured on the day of admission and on day 5 and were compared between non-survival group and survivor group. The mean value during the day of admission was found to be 34.9 and 33.05 in non-survivor and survivor group respectively. The mean value of HDL in non-survivor group on day 5 was 23.83% and 45.65% in survivor group and it was statistically significant with a p value of <0.001.

VI. Summary

The study was a hospital based observational study, aimed to study the clinical Presentation of elderly patients with Sepsis with serial monitoring of HDL cholesterol levels as a prognostic marker. 60 patients who fulfilled the inclusion criteria were studied. Available literatures both from India and abroad were reviewed and discussed with the observations made in our study.

Among 60 patients, 35 (58%) were males., 25(42%) were females

Among 60 patients 40(67%) did not survive, 20 patients survived (33%)

Most of the non survivors were hypertensive (77.5%)

Fever was the most common presenting symptom (83.3%)

Duration of hospital stay was higher in non survivors (mean (10.93)) than survivors (mean (8.1)).

Mean HDL values on the day of admission was found to be 34.9 and 33.05 in non-survivor and survivor group respectively. The mean value of HDL in non-survivor group on day 5 was 23.83% and 45.65% in survivor group and it was statistically significant. This shows that HDL value drops when sepsis is increasing and is lower in non survivors in relation to survivors.

VII. Conclusion

There is a definite correlation of HDL levels with clinical outcome of patients with sepsis.Risingtrend of HDL levels favoured improvement in clinical condition and better outcome while decreasing HDL levels implied worsening condition.

Hence HDL levels can be used as a prognostic marker in sepsis. Thus, knowledge of HDL levels of patients with sepsis can be applied to give life-saving interventions and prevent multi-organ dysfunction.

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