The Role of Plasma Lactate Dehydrogenase Testing in the Prediction of Severe Conditions in Newborn

Alshaimaa Aslman Ebeid[a*], Ahmed El-Abd Ahmed[a], Asmaa Nafady[b], Nagwan Ibrahim Ali Rashwan[a]

[a]Department of Pediatrics, Faculty of Medicine, South Valley University, Qena, Egypt.
[b]Department of Clinical and Chemical Pathology, Faculty of Medicine, South Valley University, Qena, Egypt.

Abstract

Background: Plasma lactate dehydrogenase (LDH) is found in all human cells and could be used as a biomarker to indicate poor neurodevelopment after prenatal asphyxia.

Objectives: To provide a general picture of the role of LDH in serious conditions in newborn infants admitted to the Neonatal Intensive Care Unit (NICU).

Patients and methods: A case-control study was conducted on 100 neonates (50 patients and 50 controls) at the NICU , Qena University Hospital, South Valley University, from April 2022 to December 2022. The study examined the relationship between LDH levels measured at admission and the clinical conditions of admitted newborns. LDH was measured after 12 hours of birth, allowing for analysis of its correlation with early neonatal health.

Results: The patients' group had significantly higher LDH levels (P<0.001) compared to the control group, with a median of 532.5 IU/L, and an IQR of 453.7–786.1.. The ROC curve showed that LDH has an AUC of 0.870, 80% sensitivity, 86% specificity, 85.1% PPV, and 81.1% NPV at a threshold level of > 450 IU/L, significantly distinguishing patients from controls (P < 0.001).

Conclusion: The study revealed elevated LDH levels in critically ill neonates, suggesting LDH potential as a reliable marker with good discriminatory power for identifying these patients.

Keywords: Plasma Lactate Dehydrogenase; Prediction; Severe conditions; Newborn infants.

DOI: 10.21608/SVUIJM.2024.266028.1791

***Correspondence**: shaimaaeslman@gmail.com

Received: 1 February,2024.
Revised: 1 March, 2024.
Accepted: 9 March, 2024.
Published: 7 August, 2025

Cite this article as Alshaimaa Aslman Ebeid, Ahmed El-Abd Ahmed, Asmaa Nafady, Nagwan Ibrahim Ali Rashwan. (2025). The Role of Plasma Lactate Dehydrogenase Testing in the Prediction of Severe Conditions in Newborn. SVU-International Journal of Medical Sciences. Vol.8, Issue 2, pp: 384-391.

Introduction

According to estimates from the WHO, around 15, 000 children die every day before their fifth birthday, with 46 percent of them dying during the first 28 days of life **(Oza et al., 2014; Srivastava et al., 2021).** The largest impediment to reaching the Millennium Development Goal 4 set by the United Nations in 2000 has been neonatal mortality **(Lawn et al., 2023).** The problem of newborn mortality is particularly acute in low-income nations, where 98 percent of all neonatal fatalities are documented **(Mangeret et al., 2022).** Preterm delivery problems, birth asphyxia, and/or infections have been identified as the leading causes of neonatal mortality **(Saha, 2023).**

The first few moments of life are crucial for a newborn's health and development. Unfortunately, for many infants, this period is fraught with challenges, with severe conditions like prematurity, birth asphyxia, and infections posing significant threats **(Lawn, 2018).**

Because the clinical signs of infant disorders are usually nonspecific and varied, it is more difficult to detect them early. In severe disorders, oxygen levels are low, glucose is metabolized by the anaerobic pathway, and pyruvate is then deoxidized into lactate by lactate dehydrogenase **(Anh et al., 2020).**

Thus, lactate dehydrogenase (LDH) has emerged as a potential biomarker for identifying and understanding severe conditions in neonates **(Aydin et al., 2023).** This ubiquitous enzyme, present nearly in all human tissues, plays a vital role in cellular energy metabolism **(Sun et al., 2022).** Under normal conditions, LDH levels remain within a narrow range. However, in situations of cellular stress, such as hypoxia or tissue damage, LDH is released into the bloodstream, leading to elevated plasma concentrations **(Volpe, 2020).**

This phenomenon has sparked interest in LDH's potential as a diagnostic and prognostic tool in neonatology. Previous studies have demonstrated its association with various neonatal disorders, including hypoxia-ischemic encephalopathy, sepsis, and respiratory distress syndrome **(Jobe and Bancalari, 2023).** However, the precise role of LDH in identifying and predicting the severity of these conditions remains unclear.

This study aims to demonstrate the role of plasma LDH in identifying and understanding severe conditions in newborn infants admitted to the Intensive Care Unit (NICU). We will explore the relationship between LDH levels and specific neonatal pathologies, assess its discriminatory power in differentiating critically ill newborns from healthy controls, and investigate potential correlations with clinical outcomes. By clarifying the clinical utility of LDH, we hope to contribute to improved diagnosis, and management of severe conditions in neonates, ultimately leading to better health outcomes.

Patients and methods

Study type: Case-control study.

Study setting: NICU of Qena University Hospital, South Valley University.

Study duration: 8 months from April 2022 till December 2022.

Study participants: All neonates admitted to the NICU, regardless of gestational age or gender.

Sample size: A total of 100 participants were recruited and incorporates two groups:

- **Group I (Patients, n = 50):** neonates admitted to the NICU with medical conditions necessitating intensive care.
- **Group II (Controls, n = 50):** healthy neonates with no known medical conditions, admitted for routine newborn screening or observation.

Inclusion criteria:

- All neonates (either term or preterm) of either gender with severe respiratory distress or a picture of sepsis who were admitted to the NICU at Qena University Hospital, South Valley University, in the study.

Exclusion criteria: Neonates with congenital anomalies or malformations, neonates who have been suspected of an inborn error of metabolism, or neonates with hyperbilirubinemia need

exchange.

Methods: all neonates in this study were subjected to the following:

- Complete history taking:
- Gestational age (weeks) and sex of the neonate.
- Birth weight (g) and vital signs at birth.
- Age of the neonate (days) and body weight (g) at the time of the study.
- Cause of admission.
- Duration of NICU stay.
- Complete maternal and obstetric history.
- Complete neonatal history.
- APGAR score: The components evaluated in the APGAR score (heart rate, respiratory effort, muscle tone, Moro reflex, and skin color).
- Complete a physical and clinical examination (Vital signs, assess general neonatal appearance and physicality).
- Laboratory investigations:
- **Sampling:** Blood samples were drawn from the vein between 08.00 and 10.00 AM after fasting for 12 hours. Blood samples were collected in K2 EDTA tubes for a complete blood picture (CBC), sodium fluoride tube for blood glucose measurements, heparin tube for ABG, and serum separator tube for other tests.
- **Investigations:**
  - CBC.
  - Serum glucose.
  - Serum creatinine.
  - Liver enzymes: ALT, AST.
  - Lipid profiles.
  - Arterial blood gases.
  - Serum LDH was measured after 12 hours of admission or delivery using Biosystem kits (Cat no. EKC34361-96T) (Ginper Group S.L, Spain). Normal range for total LDH in neonates is (160 to 450 IU/L).
  - Test principle: This kit depends on a sandwich ELISA assay. The plate had been pre-coated with human LDH antibodies. LDH presented in the sample was added and bound to antibodies coated on the wells. And then biotinylated human LDH Antibodies were added and bound to LDH in the sample. After incubation and washing of the wells, substrate solution was added and color develops in proportion to the amount of human LDH in the sample.

Ethical consideration: This study was approved by the Qena Faculty of Medicine ethical committee at South Valley University. Written and informed consent from all patients' parents was obtained and agreed upon for their participation in the present study. Ethical approval code: SVU-MED PED025-1-22-2-348.

Statistical analysis

The statistical analysis of the data was conducted utilizing the Statistics Package for Social Sciences (SPSS) version 24 using the Mann-Whitney U test, the chi-square test, and Pearson's correlation coefficient (r) test. Data were expressed as numbers and percentages for qualitative variables and median and interquartile range (median (IQ) for quantitative ones. A P-value < 0.05 was statistically significant. The receiver operating characteristic curve (ROC curve) was constructed to determine the discrimination poor of plasma LDH to distinguish critically ill neonates from normal.

Results

The study found a significant difference (P <0.001) in admission cause between the two groups. The median RR and SpO2 were also significantly higher in the patient group (P= 0.024) (P = 0.0001), respectively, (**Table.1**).

Table 1 . Baseline characters in the studied groups

Variable		Patients (No. = 50)	Control (No. = 50)	MW/ X^2	P-value
Sex No (%)	**Male**	23 (46%)	25 (50%)	0.16^2	0.689
	Female	27 (54%)	25 (50%)		
Age (days)	**Median (IQR)**	6 (2 – 15)	6.5 (4 – 20.25)	10.81^1	0.242

Variable		Patients (No. = 50)	Control (No. = 50)	MW/ X^2	P-value
Gestational Age (weeks)	**Median (IQR)**	36 (34 – 36.25)	36 (34 – 37)	1004.5[1]	0.079
Weight (kg)	**Median (IQR)**	2.1 (1.97 –2.5)	2.2 (2 – 2.5)	1072.5[1]	0.218
Height (cm)	**Median (IQR)**	47 (46 – 48)	47 (46 – 48)	1217.5[1]	0.819
Consanguinity	**No**	27 (54%)	30 (60%)	0.362[2]	0.545
	Yes	23 (46%)	20 (40%)		
Maturity	**Pre-term**	33 (66%)	31 (62%)	0.17[2]	0.677
	Full-term	17 (34%)	19 (38%)		
Admission	**No**	0 (0%)	28 (56%)	35.4[2]	< 0.001*
	Yes	50 (100%)	22 (44%)		
HR (beat/min)	**Median (IQR)**	140 (127.5–150)	130 (120–140)	1050.5[1]	0.159
SBP (mmHg)	**Median (IQR)**	70 (60 – 80)	70 (60 – 80)	1181[1]	0.619
DBP (mmHg)	**Median (IQR)**	50 (40 – 50)	50 (40 – 50)	1170[1]	0.539
RR (cycle/min)	**Median (IQR)**	60 (50 - 65.25)	53 (46 – 60)	924.5[1]	0.024*
SpO_2 (%)	**Median (IQR)**	90 (88 – 92)	92 (90 – 94)	758[1]	0.001*

*: significant; MW[1]: Mann Whitney U test; X2[2]: Chi-square test; HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; RR: Respiratory rate, SpO_2: oxygen saturation.

The patients group had significantly higher LDH levels (P<0.001) compared to the control group, with a median of 532.5 and an IQR of 453.7–786.1 (**Table.2**).

Table 2: laboratory investigations:

Laboratory test Median (IQR)	Patients (No. = 50)	Control (No. = 50)	MW	P-value
pH	7.32 (7.1 – 7.35)	7.33 (7.2 – 7.35)	1126	0.386
PCO2 (mmHg)	55 (38.75 – 60)	50 (38.75 -60)	1208	0.760
HCO3 (mmol/L)	19 (18 – 25)	19 (18.75 – 20.25)	1179.5	0.606
WBCs ($x10^3$/ul)	9(7 – 23.4)	7.65(6.5 – 10)	985	0.091
Hb (g/dl)	14.6(13.85 – 15.5)	14.5(14 – 17)	1229	0.884
PLTs ($x10^3$/ul)	340(233 – 573)	336(233 – 373)	1085	0.253
Creatinine (mg/dl)	0.68 (0.49 – 0.9)	0.64(0.45 – 0.84)	1132	0.415
Urea (mg/dl)	25.5(19 – 43.5)	24.5(19 – 40)	1146.5	0.474
LDH (IU/L)	532.5(453.7 – 786.1)	357(244.75 – 425)	314.5	<0.001*

*: significant; MW: Mann Whitney U test; WBCs: white blood cells; HB: hemoglobin; PLTs: platelets. CRP:C-reactive protein. LDH: lactate dehydrogenase.

The study found a significant difference in admission causes between the two groups, with 72% of patients admitted due to RDS and 28% due to sepsis, compared to 100% in the control group who required admission because of neonatal jaunduce. The patient group required more MV and CPAP for rehabilitation. The patient group saw a significant difference in outcomes (P = 0.003), with 34 (69.4%) patients discharged and 15 (30.6%) dying, compared to 100% dischareging of the control group (**Table.3**).

Table 3. Admission causes, respiratory support and outcome in the studied groups:

Variables n (%)		Patients (No. = 50)	Control (No. = 50)	X^2	P-value
Admission causes	**Respiratory distress syndrome**	36 (72%)	0 (0%)		

Variables n (%)		Patients (No. = 50)	Control (No. = 50)	X^2	P-value
	Sepsis	14 (28%)	0 (0%)	71	< 0.001*
	Neonatal jaundice	0 (0%)	50 (100%)		
Respiratory support	**Mechanical ventilation**	18 (36.7%)	0 (0%)	71	< 0.001*
	Continuous positive airway pressure	31 (63.3%)	0 (0%)		
	Off O2	0 (0%)	50 (100%)		
Outcome	**Discharged**	34 (69.4%)	50 (100%)	8.5	0.003*
	Dead	15 (30.6%)	0 (0%)		

*: significant; X2: Chi-square test.

The study found that patients on MV had significantly elevated LDH levels (median = 768.7, IQR = 494.02–1053.75) compared to those on CPAP (519.8, IQR = 452–598). Also dead patients (median = 833, IQR = 580–1257.3) compared to dischareged patients (median = 496.85, IQR = 441.9–600.75) (**Table. 4**).

Table 4. Relation Between LDH Concentration and admission causes, blood culture, respiratory support, and outcome:

Variables		LDH in patients (No = 50)	MW	P-value
Admission causes	**RDS (n =36)**	525 (465.3 – 786.1)	71	< 0.001*
	Sepsis (n =14)	559 (439.5 – 1189.25)		
Blood culture	**Negative (n = 36)**	525 (466 – 817.37)	229	0.619
	Sepsis (n = 14)	586.5 (400.1 – 790)		
Respiratory support	**MV (n = 18)**	768.7 (494.02 - 1053.75)	179	0.038 *
	CPAP (n = 31)	519.8 (452 – 598)		
Outcome	**Discharged (n = 35)**	496.85 (441.9 – 600.75)	99	0.001 *
	Dead (n = 15)	833 (580 – 1257.3)		

*: significant; MW: Mann Whitney U test, RDS: respiratory distress syndrome. MV: mechanical ventilation; CPAP: continuous positive airway pressure.

LDH can be used in differentiation between the patients' group and the control group at a cutoff level of > 450 IU/L, with 80% sensitivity, 86% specificity, 85.1% PPV, and 81.1% NPV (AUC = 0.87, p-value < 0.001) (**Table 5, Fig.1**).

Table 5. Diagnostic performance of serum LDH in studied newborn disorders:

Variables	Cut off	AUC	Sensitivity	Specificity	PPV	NPV	p-value
LDH (IU/L)	> 450	0.870	80%	86%	85.10%	81.10%	< 0.001

PPV: positive predictive value; AUC: Area under curve; NPV: negative predictive value.

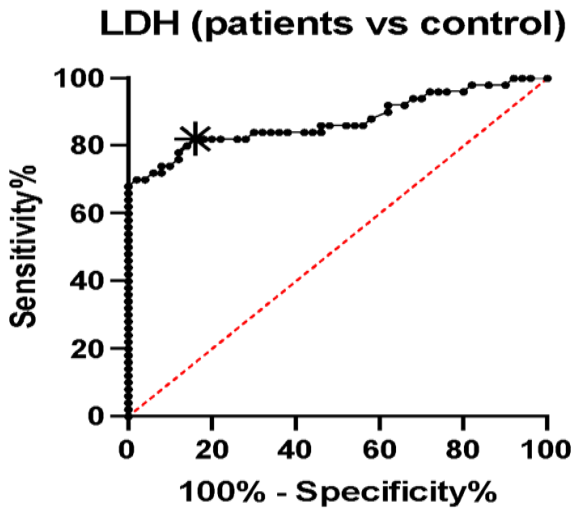

Fig.1. ROC curve of serum LDH in the studied group.

We found a statistically significant positive correlation between LDH, creatinine (r= 0.39; P = 005), and urea (r= 0.41; P=0.003) and a statistically significant negative correlation between LDH and SpO2 (r= -0.43; P=0.002) (**Table.6**).

Table 6: Relation between LDH and other parameters in the studied groups

LDH	Patients group		Control group	
	r	p-value	r	p-value
Age	0.09	0.534	-0.24	0.089
Gestational Age	-0.02	0.898	-0.08	0.591
Weight	-0.03	0.832	0.11	0.452
Height	-0.02	0.903	-0.06	0.677
Heart rate	0.06	0.662	**0.36**	**0.01***
Systolic Blood Pressure	0.06	0.705	-0.02	0.878
Diastolic Blood Pressure	0.12	0.422	0.11	0.468
Respiratory Rate	0.07	0.61	**0.43**	**0.002***
Oxygen Saturation (SpO2)	**-0.43**	**0.002***	-0.16	0.264
Serum Creatinine	**0.39**	**0.005***	0.16	0.26
Serum Urea	**0.41**	**0.003***	0.28	0.051
C-Reactive protein	-0.07	0.627	-0.16	0.263
pH	-0.02	0.872	-0.08	0.562
pCO2	-0.02	0.892	-0.02	0.877
HCO3	-0.21	0.142	-0.06	0.698
White Blood Cells count	0.03	0.815	0.26	0.074
Hemoglobin	-0.07	0.65	-0.22	0.127
Platelet count	0.01	0.949	0.19	0.179

*: significant; r: Pearson correlation coefficient.

Discussion

The results of this study provide a valuable demonstration of the potential role of LDH as a diagnostic and prognostic biomarker for severe conditions in newborn infants. The elevated LDH levels observed in critically ill neonates compared to healthy controls suggest its potential utility in identifying and stratifying

neonatal health risks. The following discussion will investigate the implications of these findings, explore potential mechanisms underlying the observed correlations, and address the broader context of LDH as a biomarker in neonatology.

The patient group had a higher RR (60 cycles/min) and lower SpO2 (90%) compared to the control group RR (53 cycles/min) SpO2 (92%). The patient group had a higher median LDH level (532.5), with a significant difference between the two groups (P<0.001). These findings are consistent with previous research by **Ton et al.(2020).**

There were several studies on serum LDH levels in many infections. **Francesco et al.(2009),** demonstrated that serum LDH levels were significantly elevated in neonates with necrotizing enterocolitis ($p < 0.005$). The study by **Zein et al.(2004**), and **Algebaly et al.(2021),** detected increased plasma LDH levels in serious infections as a marker of tissue damage but did not improve LDH levels at 48 hours as a major predictor of mortality in patients with severe sepsis.

In our study, the median LDH level was 768.7 in the 18 (36.7%) patients who required MV and 519.8 in the 31 (63.3%) patients who required CPAP for respiratory support. These results align with **Ton et al.(2020)** findings.

The observed correlation between LDH levels and admission causes, such as RDS and sepsis, aligns with previous research indicating a relationship between elevated LDH and adverse clinical conditions in neonates **(Ton et al., 2020; Mohamed et al., 2021).**

ROC curve analysis showed LDH's high sensitivity and specificity in distinguishing patient and control groups, with a cutoff level of >450 IU/L, highlighting its potential in diagnosing critical pediatric patients. This was in line with **(Algebaly et al., 2021).**

The positive correlations between LDH, HR, and RR, along with the negative correlation with SO2, further support the notion that LDH levels may reflect the physiological stress and severity of neonatal conditions. These correlations align with the results obtained by **Servet et al.(2013),** who demonstrated a positive relationship between LDH levels and the duration of oxygen therapy.

The elevated mortality rate in the patient group, coupled with the findings of **Ton et al.(2020),** supports the notion that plasma LDH levels may be indicative of poor outcomes in neonates with serious conditions.

Conclusion

This study validates LDH's role in predicting severe conditions in newborns admitted to the NICU, and detecting elevated levels in critically ill neonates. Correlations with oxygen saturation and kidney function markers suggest respiratory and renal impairment.

List Of Abbreviation

Abbreviations	Full Term
AUC	Area Under the curve
AUC	Area Under The Curve
CPAP	Continuous Positive Airway Pressure
IQR	Interquartile Range
LDH	Lactate Dehydrogenase
MV	Mechanical Ventilation
MW	Mann Whitney U Test
NICU	Neonatal Intensive Care Unit
NPV	Negative Predictive Value
PPV	Positive Predictive Value
r	Pearson Correlation Coefficient
RDs	Respiratory Distress Syndrome
ROC	Receiver Operative Characteristic Curve
SPSS	Statistic Package for Social Sciences
X2	Chi-Square Test

References

- **Algebaly HF, Abd-Elal A, Kaffas RE, Ahmed ES. (2021).** Predictive value of serum lactate dehydrogenase in diagnosis of septic shock in critical pediatric patients: A cross-sectional study. Journal of Acute Disease, 10(3): 107-111.
- **Anh T, Hao TK, Hoang HH. (2020).** The role

of plasma lactate dehydrogenase testing in the prediction of severe conditions in newborn infants: A prospective study. Research and Reports in Neonatology, 1(1): 31-35.

- **Aydin S, Tulek B, Karaali Z. (2023).** Early predictive value of plasma lactate dehydrogenase and N-terminal pro-brain natriuretic peptide levels in neonatal hypoxic-ischemic encephalopathy. Pediatric Research, 84(4): 609-616.
- **Francesco M, Maria PR, Pietro B. (2009).** Increased serum activity of lactate dehydrogenase in infants with necrotising enterocolitis: a potential marker of advanced disease. Paediatrics and Child Health.;19(1):S60-S64.
- **Jobe AH, Bancalari HW. (2023).** Neonatal respiratory distress syndrome. New England Journal of Medicine, 388(8): 746-758.
- **Lawn J. (2018).** Rethinking interventions to improve preterm survival: the WHO Antenatal Corticosteroids for Preterm Birth Initiative. Lancet Glob Health, 6(4): 407-424.
- **Lawn JE, Bhutta ZA, Ezeaka C, Saugstad O. (2023).** Ending preventable neonatal deaths: multicountry evidence to inform accelerated progress to the sustainable development goal by 2030. Neonatology, 120(4): 491-499.
- **Mangeret F, Benski AC, Golaz A, Zala PZ, Kyokan M, Wagner N, et al. (2022).** 2.5 million annual deaths—are neonates in low-and middle-income countries too small to be seen? A bottom-up overview on neonatal Morbi-mortality. Tropical medicine and infectious disease, 7(5): 64-72.
- **Meng L, Hao L, Xuechun J, Mengqi J, Xun Z, Gengtao F, et al. (2021).** Gd-induced electronic structure engineering of a NiFe-layered double hydroxide for efficient oxygen evolution. Journal of Materials Chemistry, 9(5): 2999-3006.
- **Mohamed SE, Ghada MA, Haidy K, Sally A. (2021).** Novel predictor markers for early differentiation between transient tachypnea of newborn and respiratory distress syndrome in neonates. International Journal of Immunopathology and Pharmacology, 35: 1-10
- **Oza S, Cousens SN, Lawn JE. (2014).** Estimation of daily risk of neonatal death, including the day of birth, in 186 countries in 2013: a vital-registration and modelling-based study. The Lancet Global health, 2(11): 635-644.
- **Sachin Ch, Rupa RS, Nisha KB. (2019).** Lactate dehydrogenase and CK-MB as predictors of hypoxic ischaemic encephalopathy in newborns with perinatal asphyxia. MedPulse International Journal of Pediatrics, 11(2): 58-64.
- **Saha U. (2023).** Neonatal Mortality and Morbidity: The Burden. In Clinical Anesthesia for the Newborn and the Neonate (pp. 3-10). Singapore: Springer Nature Singapore.
- **Servet O, Zeynel G, Saltuk BB, Hasan K, Deniz O, Ahmet S. (2013).** Lactate and lactate dehydrogenase in predicting the severity of transient tachypnea of the newborn. The Journal of Maternal-Fetal & Neonatal Medicine, 26(12): 1245-1248.
- **Srivastava S, Upadhyay SK, Chauhan S, Alagarajan M. (2021).** Preceding child survival status and its effect on infant and child mortality in India: An evidence from National Family Health Survey 2015–16. BMC Public Health, 21(1): 15-77.
- **Sun Z, Yang M, Wang W. (2022).** Diagnostic and prognostic value of lactate dehydrogenase in neonates with sepsis: a meta-analysis. Journal of Pediatric Surgery, 57(12): 2405- 2413.
- **Ton NV, Tran KH, Huynh HH. (2020).** The role of plasma lactate dehydrogenase testing in the prediction of severe conditions in newborn infants: A prospective study. Research and Reports in Neonatology, 10:31-35.
- **Volpe NJ. (2020).** Hypoxic-ischemic encephalopathy in newborn infants. Clinics in Perinatology, 47(3): 229-254.
- **Zein JG, Lee GL, Tawk M, Dabaja M, Kinasewitz GT. (2004)**. Prognostic significance of elevated serum lactate dehydrogenase (LDH) in patients with severe sepsis. CHEST Journal, 12(6): 873-877.