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Date of Search: 10 Aug 2017

Sources Searched: Medline, Embase, DynaMed Plus.

Lactate Reference Ranges in Sepsis

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Evidence Summary:

Historically, determining appropriate endpoints for fluid resuscitation in severe sepsis and septic shock have proved to be challenging. The current [Surviving Sepsis Campaign, 2016](#) guidelines recommend patients with an initial blood lactate level twice above the normal limit (≥ 4 mmol/L) to be promptly resuscitated. This trigger point is also endorsed by the [RCOG Bacterial Sepsis in Pregnancy](#) Green-Top Guideline(2012), stating that a serum lactate ≥ 4 mmol/l is indicative of tissue hypoperfusion.

The threshold of > 4 mmol/l was first used as a cut off in the landmark *Early goal-directed therapy in the treatment of severe sepsis and septic shock* trial ([Rivers, 2001](#)) and again for the more recent [ProMISe](#), [ProCESS](#), and [ARISE](#) trials.

The validity of this cut off has however been called into question by studies which have shown that patients with [intermediate concentrations of lactate \(2-4 mmol/L\)](#) or those within a [high end of the normal range \(1.4-2.3 mmol/L\)](#) have a poorer prognosis when compared with patients with low or normal lactate concentrations. In the absence of large scale studies the optimal lactate cut off which should trigger resuscitation remains unclear.

1. Blood Lactate Levels Cutoff and Mortality Prediction in Sepsis-Time for a Reappraisal? a Retrospective Cohort Study.

Author(s): Filho, Roberto Rabello; Rocha, Leonardo Lima; Corrêa, Thiago Domingos; Pessoa, Camila Menezes Souza; Colombo, Giancarlo; Assuncao, Murillo Santucci Cesar

Source: Shock (Augusta, Ga.); Nov 2016; vol. 46 (no. 5); p. 480-485

Publication Date: Nov 2016

Publication Type(s): Journal Article

PubMedID: 27380535

Available in full text at [Shock](#) - from Ovid

Abstract:The objective of this study was to identify the initial value of blood lactate that best correlates with 28-day mortality in resuscitated septic shock patients. This was a retrospective cohort study including 443 patients admitted to an intensive care unit (ICU) with severe sepsis or septic shock from the emergency department. A receiver-operating characteristic (ROC) curve was drawn to obtain the best cutoff value for initial blood lactate associated with 28-day mortality. Patients were then dichotomized according to the chosen lactate cutoff, and sensitivity, specificity, and positive and negative predictive values were calculated. Baseline blood lactate level more than 2.5 mmol/L showed the largest area under the ROC curve to predict 28-day mortality (ROC area, 0.70; 95% confidence interval [CI], 0.62-0.79), with sensitivity, specificity, and negative predictive value of 67.4%, 61.7%, and 94.2%, respectively. Mortality at 28 days was 16.9% (31/183) in patients with initial lactate more than 2.5 mmol/L and 5.8% (15/260) in patients with initial lactate at most 2.5 mmol/L (relative risk, 2.93; 95% CI, 1.63-5.28; $P < 0.001$). Initial blood lactate levels more than 2.5 mmol/L (hazard ratio [HR], 2.86; 95% CI, 1.53-5.33; $P = 0.001$) and Sepsis-related Organ Failure Assessment score at ICU admission (HR, 1.18; 95% CI, 1.09-1.27; $P < 0.001$) were associated with increased 28-day mortality in the adjusted Cox regression. In this retrospective cohort study, a lactate level more than 2.5 mmol/L was the best threshold to predict 28-day mortality among severe sepsis and septic shock patients. Further prospective studies should address the impact on morbidity and mortality of this threshold as a trigger to resuscitation in this population of critically ill patients.

Database: Medline

2. A study to determine the normal concentrations of serum procalcitonin (PCT), plasma lactate and serum C-reactive protein (CRP) following normal parturition in low risk women

Author(s): Orr K.; McSwiggan S.; Strachan J.; Marwick C.; Nicoll A.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Jun 2016; vol. 123 ; p. 62-63

Publication Date: Jun 2016

Publication Type(s): Conference Abstract

Available in full text at [BJOG: An International Journal of Obstetrics and Gynaecology](#) - from John Wiley and Sons

Abstract: Introduction Sepsis is a major contributor to maternal and perinatal morbidity and mortality. Early recognition of sepsis can improve clinical outcomes. Non-specific inflammatory markers such as lactate and CRP are now routinely used for diagnosing intra-partum sepsis. PCT is considered to be a more specific marker for bacterial sepsis. Parturition is an inflammatory process and could potentially influence concentrations of maternal inflammatory markers. Objective To establish normal ranges for PCT, lactate and CRP for normal parturition in low risk women. Methods Data were collected prospectively from a cohort of low risk women in spontaneous labour at term. Samples were obtained within 1 hour of normal birth. Samples were analysed blind at the on-site biochemistry laboratory. Based on international standards for non pregnant women, elevated PCT was defined as > 0.5 ng/mL, elevated lactate was defined as > 2 mmol/L and elevated CRP was defined as > 10 mg/L. The local Maternity Database was examined to confirm that none of these women went on to develop sepsis in the 7 days following delivery. Results Samples were taken from 118 women. 33/118 (28%) were nulliparous. Median maternal age = 29 years (range = 19-40 years). Median BMI = 24 kg/m² (range = 17-35 kg/m²). Median PCT = 0.07 ng/mL (range = 0-0.22 ng/mL). 0/118 (0%) had an elevated PCT. Median lactate = 2.5 mmol/L (range = 0.9-8.5 mmol/L). 80/118 (67.8%) had an elevated lactate. 22/118 (18.7%) had a lactate >4.0 mmol/L. Median CRP = 8 mg/L (range = 0-84 mg/L). 46/118 (39.0%) had an elevated CRP. Conclusion Normal labour does not affect maternal PCT concentrations. However normal parturition is associated with increases in maternal lactate and CRP. In the absence of infection a significant number of low risk women will have a lactate concentration greater than the current RCOG standard for sepsis recognition. In the absence of clinical signs or features of sepsis, elevated CRP and lactate should not be considered as diagnostic of maternal infection. During parturition PCT appears to be a better marker for excluding infection and consideration should be given to incorporate PCT into obstetric practice to allow the prompt recognition of intra-partum sepsis. Using PCT to diagnose obstetric sepsis might reduce the number of women and their infants receiving antibiotics unnecessarily. This potentially could reduce antibiotic resistance, enhance patient safety and reduce costs for the NHS.

Database: EMBASE

3. Reference values for clinical chemistry tests during normal pregnancy.

Author(s): Larsson, A; Palm, M; Hansson, L-O; Axelsson, O

Source: BJOG : an international journal of obstetrics and gynaecology; Jun 2008; vol. 115 (no. 7); p. 874-881

Publication Date: Jun 2008

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 18485166

Available in full text at [BJOG: An International Journal of Obstetrics and Gynaecology](#) - from John Wiley and Sons

Abstract:OBJECTIVE Reference values are usually defined based on blood samples from healthy men or nonpregnant women. This is not optimal as many biological markers changes during pregnancy and adequate reference values are of importance for correct clinical decisions. There are only few studies on the variations of laboratory tests during normal pregnancies, especially during the first two trimesters. It is thus a need to establish such reference values.DESIGNLongitudinal study of laboratory markers in normal pregnancies.SETTINGUppsala University Hospital, Sweden.POPULATIONHealthy pregnant females.METHODSWe have studied 25 frequently used laboratory tests during 52 normal pregnancies. Each woman was sampled up to nine times and the samples were divided according to collection time into the following groups: gestational week 7-17; week 17-24; week 24- 28; week 28-31; week 31-34; week 34-38; predelivery (0-2 weeks before delivery) and postpartum (> 6 weeks after delivery). The 2.5 and 97.5 percentiles for these markers were calculated according to the recommendations of the International Federation of Clinical Chemistry on the statistical treatment of reference values.RESULTSReference intervals are reported for plasma alanine aminotransferase, albumin, alkaline phosphatase, pancreas amylase, apolipoprotein A1, apolipoprotein B, aspartate aminotransferase, bilirubin, calcium, chloride, creatinine, cystatin C, ferritin, gamma-glutamyltransferase, iron, lactate dehydrogenase, magnesium, phosphate, potassium, sodium, transferrin, triglycerides, thyroid-stimulating hormone, urate and urea during these pregnancy periods.CONCLUSIONS Most of the analytes change during normal pregnancy. It is thus of importance to use special reference values during pregnancy.

Database: Medline

4. Pregnancy and laboratory studies: a reference table for clinicians.

Author(s): Abbassi-Ghanavati, Mina; Greer, Laura G; Cunningham, F Gary

Source: Obstetrics and gynecology; Dec 2009; vol. 114 (no. 6); p. 1326-1331

Publication Date: Dec 2009

Publication Type(s): Journal Article Review

PubMedID: 19935037

Available in full text at [Obstetrics and gynecology](#). - from Ovid

Abstract:OBJECTIVETo establish normal reference ranges during pregnancy for common laboratory analytes.DATA SOURCESWe conducted a comprehensive electronic database review using PUBMED and MEDLINE databases. We also reviewed textbooks of maternal laboratory studies during uncomplicated pregnancy.METHODS OF STUDY SELECTION We searched the databases for studies investigating various laboratory analytes at various times during pregnancy. All abstracts were examined by two investigators and, if they were found relevant, the full text of the article was reviewed. Articles were included if the analyte studied was measured in pregnant women without major medical problems or confounding conditions and if the laboratory marker was measured and reported for a specified gestational age.TABULATION, INTEGRATION, AND RESULTSFor each laboratory marker, data were extracted from as many references as possible, and these data were combined to establish normal reference ranges in pregnancy. When possible, the 2.5 and 97.5 percentiles were reported as the normal range. In some of the reference articles, however, the reported range was based on the minimum and maximum value of the laboratory constituent. In those cases, the minimum to maximum range was used and combined with the 2.5 and 97.5 percentile range. We found that there is a substantial difference in normal values in some laboratory markers in the pregnant state when compared with the nonpregnant state.CONCLUSIONIt is important to consider normal reference ranges specific to pregnancy when interpreting some laboratory results that may be altered by the normal changes of pregnancy.

Database: Medline

5. Towards a consensus definition of maternal sepsis: results of a systematic review and expert consultation.

Author(s): Bonet, Mercedes; Nogueira Pileggi, Vicky; Rijken, Marcus J; Coomarasamy, Arri; Lissauer, David; Souza, João Paulo; Gülmezoglu, Ahmet Metin

Source: Reproductive health; May 2017; vol. 14 (no. 1); p. 67

Publication Date: May 2017

Publication Type(s): Journal Article Review

PubMedID: 28558733

Available in full text at [Reproductive Health](#) - from BioMed Central

Abstract:BACKGROUND There is a need for a clear and actionable definition of maternal sepsis, in order to better assess the burden of this condition, trigger timely and effective treatment and allow comparisons across facilities and countries. The objective of this study was to review maternal sepsis definitions and identification criteria and to report on the results of an expert consultation to develop a new international definition of maternal sepsis. METHODS All original and review articles and WHO documents, as well as clinical guidelines providing definitions and/or identification criteria of maternal sepsis were included. A multidisciplinary international panel of experts was surveyed through an online consultation in March-April 2016 on their opinion on the existing sepsis definitions, including new definition of sepsis proposed for the adult population (2016 Third International Consensus Definitions for Sepsis and Septic Shock) and importance of different criteria for identification of maternal sepsis. The definition was agreed using an iterative process in an expert face-to-face consensus development meeting convened by WHO and Jhpiego. RESULTS Standardizing the definition of maternal sepsis and aligning it with the current understanding of sepsis in the adult population was considered a mandatory step to improve the assessment of the burden of maternal sepsis by the expert panel. The literature review and expert consultation resulted in a new WHO consensus definition "Maternal sepsis is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, child-birth, post-abortion, or post-partum period". Plans are in progress to validate the new WHO definition of maternal sepsis in a large international population. CONCLUSION The operationalization of the new maternal sepsis definition requires generation of a set of practical criteria to identify women with sepsis. These criteria should enable clinicians to focus on the timely initiation of actionable elements of care (administration of antimicrobials and fluids, support of vital organ functions, and referral) and improve maternal outcomes.

Database: Medline

6. New clinical criteria for septic shock: serum lactate level as new emerging vital sign.

Author(s): Lee, Su Mi; An, Won Suk

Source: Journal of thoracic disease; Jul 2016; vol. 8 (no. 7); p. 1388-1390

Publication Date: Jul 2016

Publication Type(s): Journal Article Comment

PubMedID: 27501243

Available in full text at [Journal of Thoracic Disease](#) - from National Library of Medicine

Database: Medline

7. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Author(s): Rhodes A.; Evans L.E.; Nunnally M.E.; Alhazzani W.; Rochwerf B.; Levy M.M.; Antonelli M.; Ferrer R.; Kumar A.; Sevransky J.E.; Coopersmith C.; Sprung C.L.; Rubenfeld G.D.; Angus D.C.; Annane D.; Beale R.J.; Bellingham G.J.; Bernard G.R.; Chiche J.-D.; De Backer D.P.; French C.J.; Fujishima S.; Gerlach H.; Hidalgo J.L.; Hollenberg S.M.; Schorr C.A.; Dellinger R.P.; Jones A.E.; Karnad D.R.; Kleinpell R.M.; Plunkett C.M.; Koh Y.; Lisboa T.C.; Machado F.R.; Marini J.J.; Marshall J.C.; Mazuski J.E.; Osborn T.M.; McIntyre L.A.; McLean A.S.; Mehta S.; Moreno R.P.; Myburgh J.; Navalesi P.; Nishida O.; Perner A.; Ranieri M.; Seckel M.A.; Seymour C.W.; Shieh L.; Shukri K.A.; Simpson S.Q.; Singer M.; Thompson B.T.; Townsend S.R.; Van der Poll T.; Wiersinga W.J.; Vincent J.-L.; Zimmerman J.L.

Source: Intensive Care Medicine; Mar 2017; vol. 43 (no. 3); p. 304-377

Publication Date: Mar 2017

Publication Type(s): Article

PubMedID: 28101605

Available in full text at [Intensive Care Medicine](#) - from Springer Link Journals

Abstract:Objective: To provide an update to "Surviving Sepsis Campaign Guidelines for Management of Sepsis and Septic Shock: 2012". Design: A consensus committee of 55 international experts representing 25 international organizations was convened. Nominal groups were assembled at key international meetings (for those committee members attending the conference). A formal conflict-of-interest (COI) policy was developed at the onset of the process and enforced throughout. A stand-alone meeting was held for all panel members in December 2015. Teleconferences and electronic-based discussion among subgroups and among the entire committee served as an integral part of the development. Methods: The panel consisted of five sections: hemodynamics, infection, adjunctive therapies, metabolic, and ventilation. Population, intervention, comparison, and outcomes (PICO) questions were reviewed and updated as needed, and evidence profiles were generated. Each subgroup generated a list of questions, searched for best available evidence, and then followed the principles of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to assess the quality of evidence from high to very low, and to formulate recommendations as strong or weak, or best practice statement when applicable. Results: The Surviving Sepsis Guideline panel provided 93 statements on early management and resuscitation of patients with sepsis or septic shock. Overall, 32 were strong recommendations, 39 were weak recommendations, and 18 were best-practice statements. No recommendation was provided for four questions. Conclusions: Substantial agreement exists among a large cohort of international experts regarding many strong recommendations for the best care of patients with sepsis. Although a significant number of aspects of care have relatively weak support, evidence-based recommendations regarding the acute management of sepsis and septic shock are the foundation of improved outcomes for these critically ill patients with high mortality. Copyright © 2017, SCCM and ESICM.

8. Lactic acid measurement to identify risk of morbidity from sepsis in pregnancy.

Author(s): Albright, Catherine M; Ali, Tariq N; Lopes, Vrishali; Rouse, Dwight J; Anderson, Brenna L

Source: American journal of perinatology; Apr 2015; vol. 32 (no. 5); p. 481-486

Publication Date: Apr 2015

Publication Type(s): Journal Article

PubMedID: 25486284

Abstract:OBJECTIVE This study aims to assess the risk of morbidity associated with maternal lactic acid concentration in women with possible sepsis in pregnancy.STUDY DESIGNRetrospective cohort of pregnant and postpartum patients with signs of sepsis. Morbidity outcomes were compared by lactic acid concentration. Linear regression was used to evaluate the association between lactic acid and adverse outcomes.RESULTSOut of the 850 women included, 159 had lactic acid measured. Patients with lactic acid measured had higher morbidity: positive blood cultures (16.8 vs. 5.5%, $p = 0.04$), admission to the intensive care unit (5 vs. 0.1%, $p < 0.01$) or acute monitoring unit (17.2 vs. 0.9%, $p < 0.01$), longer hospital stay (median 3 vs. 2 days, $p < 0.01$), and preterm delivery (18.3 vs. 10.9%, $p = 0.05$). The mean lactic concentration was higher in patients admitted to the intensive care (2.6 vs. 1.6 mmol/L, $p = 0.04$) and telemetry unit (2.0 vs. 1.6, $p = 0.03$), and in those with positive blood cultures (2.2 vs. 1.6, $p < 0.01$). Lactic acid was positively associated with intensive care or telemetry unit admission, adjusted odds ratio per 1 mmol/L increase in lactic acid 2.34 (95% confidence interval, 1.33-4.12).CONCLUSIONElevated lactic acid in pregnancy is associated with adverse maternal outcomes from presumed sepsis. In this cohort, lactic acid measurement was a marker of more severe infection.

Database: Medline

9. Multicenter implementation of a treatment bundle for patients with sepsis and intermediate lactate values

Author(s): Liu V.X.; Escobar G.J.; Morehouse J.W.; Marelich G.P.; Soule J.; Russell T.; Whippy A.; Skeath M.; Adams C.

Source: American Journal of Respiratory and Critical Care Medicine; Jun 2016; vol. 193 (no. 11); p. 1264-1270

Publication Date: Jun 2016

Publication Type(s): Article

PubMedID: 26695114

Available in full text at [American Journal of Respiratory and Critical Care Medicine](#) - from ProQuest

Abstract:Rationale: Treatments for patients with sepsis with intermediate lactate values (>2 and <4 mmol/L) are poorly defined. Objectives: To evaluate multicenter implementation of a treatment bundle (including timed intervals for antibiotics, repeat lactate testing, and intravenous fluids) for hemodynamically stable patients with sepsis and intermediate lactate values in the emergency department. Methods: We evaluated patients in annual intervals before and after bundle implementation in March 2013. We evaluated bundle compliance and compared outcome measures across groups with multivariable logistic regression. Because of their perceived risk for iatrogenic fluid overload, we also evaluated patients with a history of heart failure and/or chronic kidney disease. Measurements and Main Results: We identified 18,122 patients with sepsis and intermediate lactate values, including 36.1% treated after implementation. Full bundle compliance increased from 32.2% in 2011 to 44.9% after bundle implementation ($P = 0.01$). Hospital mortality was 8.8% in 2011, 9.3% in 2012, and 7.9% in 2013 ($P = 0.02$). Treatment after bundle implementation was associated with an adjusted hospital mortality odds ratio of 0.81 (95% confidence interval, 0.66-0.99; $P = 0.04$). Decreased hospital mortality was observed primarily in patients with a heart failure and/or

kidney disease history (P,0.01) compared with patients without this history (P,0.40). This corresponded to notable changes in the volume of fluid resuscitation in patients with heart failure and/or kidney disease after implementation. Conclusions: Multicenter implementation of a treatment bundle for patients with sepsis and intermediate lactate values improved bundle compliance and was associated with decreased hospital mortality. These decreases were mediated by improved mortality and increased fluid administration among patients with a history of heart failure and/or chronic kidney disease.

Database: EMBASE

10. Evaluation of point-of-care maternal venous lactate testing in normal pregnancy.

Author(s): Maguire, Patrick J; Finlay, Janna; Power, Karen A; Harley, Ruth; Mhurchú, Muireann Ní; Sheehan, Sharon R; Fanning, Rebecca A; Turner, Michael J

Source: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; 2016; vol. 29 (no. 16); p. 2607-2610

Publication Date: 2016

Publication Type(s): Journal Article Evaluation Studies

PubMedID: 26456421

Abstract:OBJECTIVEThere is little information about whether the established non-pregnant adult venous lactate reference range is appropriate for pregnancy. This prospective observational study examined whether the non-pregnant adult reference range is appropriate during pregnancy.METHODSWomen attending for routine prenatal appointments or elective cesarean delivery in a tertiary hospital were recruited. Clinical details were recorded and venous lactate concentration was measured using a point-of-care (POC) device.RESULTSO f the 246 women, 199 were 6-18 weeks' gestation and 47 were 36-42 weeks' gestation. Mean lactate concentration was within the non-pregnant reference range in early and late pregnancy ($0.86 \text{ SD} \pm 0.46 \text{ mmol/L}$ and $1.15 \text{ SD} \pm 0.40 \text{ mmol/L}$, respectively). The mean time between phlebotomy and result was $6.1 \text{ SD} \pm 1.7 \text{ min}$. There was no correlation between lactate levels and either maternal age or time interval from tourniquet placement to lactate measurement. In women of 6-18 weeks' gestation positive bivariate relationships were found between lactate and BMI ($p = 0.03$, $r = 0.158$), earlier gestational age ($p = 0.04$, $r = -0.145$), and smoking ($p = 0.01$, $r = 0.183$), but these were not found in late pregnancy.CONCLUSIONSThe venous lactate reference range for the non-pregnant adult may be applied in pregnancy. Further studies should examine lactate dynamics in labor and postpartum.

Database: Medline

11. Clinical predictors of adverse outcome in severe sepsis patients with lactate 2-4 mM admitted to the hospital.

Author(s): Tang, Y; Choi, J; Kim, D; Tudtud-Hans, L; Li, J; Michel, A; Baek, H; Hurlow, A; Wang, C; Nguyen, H B

Source: QJM : monthly journal of the Association of Physicians; Apr 2015; vol. 108 (no. 4); p. 279-287

Publication Date: Apr 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 25193540

Available in full text at [QJM](#) - from Highwire Press

Available in full text at [QJM: An International Journal of Medicine](#) - from Oxford University Press ;
Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Abstract:BACKGROUND Severe sepsis patients with initial lactate level 2-4 mM are commonly considered to have lower risk for mortality and adverse outcomes. AIM We aim to determine clinical variables that are associated with adverse outcome in these patients. DESIGN A retrospective cohort study. METHODS Severe sepsis patients with initial lactate ≥ 2 and < 4 mM admitted to our hospital were examined for any of the following primary outcomes: (i) in-hospital death, (ii) vasopressor requirement, (iii) use of mechanical ventilator, (iv) lactate ≥ 4.0 mM or (v) need care in the intensive care unit (ICU) within 48 h. RESULTS Five-hundred and thirty-five patients were enrolled, age 58.7 ± 19.3 years, 53.2% male. The most common sources of infection were urinary tract infection and pneumonia, 38.3 and 35.7%, respectively. One-hundred and twenty-four (23.2%) patients had at least one primary adverse outcome within 48 h, including in-hospital death 1.1%, vasopressor requirement 12.9%, use of mechanical ventilator 13.3%, increase lactate ≥ 4.0 mM in 5.6% patients and 21.5% of patients requiring ICU (including 13.8% of the patients admitted directly to ICU from the emergency department, and 7.7% initially admitted to the general medical ward but later required ICU transfer). Altered mentation, hypotension, tachypnea and elevated blood urea nitrogen at admission were associated with the primary outcome in multivariable logistic regression analysis, odds ratio 2.50 (95% confidence interval: 1.54, 4.06), 3.76 (2.31, 6.10), 1.97 (1.22, 3.17) and 1.78 (1.11, 2.83), respectively. CONCLUSIONS Our study suggests that clinicians should be cautious about the potential adverse outcomes in severe sepsis patients with initial lactate level between 2 and 4 mM and a presentation of altered mentation, hypotension, tachypnea and/or elevated blood urea nitrogen.

Database: Medline

12. Clinical chorioamnionitis at term VII: The maternal serum lactate concentrations

Author(s): Romero R.; Chaemsaitong P.; Docheva N.; Korzeniewski S.J.; Chaivasit N.; Tarca A.L.; Kusanovic J.P.; Dong Z.; Yoon B.H.; Hassan S.S.; Chaiworapongsa T.; Yeo L.

Source: Journal of Perinatal Medicine; Oct 2015; vol. 43

Publication Date: Oct 2015

Publication Type(s): Conference Abstract

Abstract:Objective: Plasma lactate is a marker of sepsis. Since clinical chorioamnionitis is the most common pregnancy related systemic infection, the objective of this study is to determine maternal serum lactate concentration in patients with clinical chorioamnionitis at term according to the presence or absence of intra-amniotic inflammation and the presence of proven detectable bacteria in the amniotic cavity. Materials and methods: A retrospective cross-sectional study was conducted and participants from the following groups were included: 1) uncomplicated pregnancy at term with and without spontaneous labor (n=95, n=83, respectively); and 2) clinical chorioamnionitis at term (n=43). Transabdominal amniocentesis was performed. Women with clinical chorioamnionitis were classified according to the results of amniotic fluid culture, broad-range polymerase chain reaction coupled with electrospray ionization mass spectrometry (PCR/ESI-MS), and amniotic fluid interleukin (IL)-6 concentration into three groups: 1) no intra-amniotic inflammation; 2) intra-amniotic inflammation without detectable microorganisms; or 3) microbial-associated intra-amniotic inflammation. The maternal serum concentrations of L-Lactate were determined with sensitive and highly selective assays (Abcam, MA, USA). Results: 1) There is no difference in the median [IQR (interquartile range)] maternal serum lactate concentrations (mmol/L) between patients with and without spontaneous labor at term [term in labor: 7.8 (5.4-10.5) vs. term no labor: 7.5 (4.8-8.7); p=0.09] (Figure A); 2) patients with clinical chorioamnionitis at term had significantly higher median maternal serum lactate concentrations (mmol/L) than those with spontaneous labor at term [clinical chorioamnionitis at term: 9.4 (6.7- 11.9) vs. term in labor: 7.8 (5.4-10.5); p<0.001] (Figure A); 3) the median maternal serum lactate concentrations (mmol/L) were significantly higher in patients with clinical chorioamnionitis at term who had microbial-associated intra-amniotic inflammation (also known as intra-amniotic infection) than in those without intra-amniotic inflammation [microbial-associated intra-amniotic inflammation: 10.1 (8.2-13.1) vs. no intra-amniotic inflammation: 7.5 (6.0-8.7); p=0.04] (Figure B); and 4) there were no significant differences in the median maternal serum lactate concentrations between patients with intra-amniotic inflammation with and without demonstrable microorganisms (p=0.97) (Figure B). Conclusion: This is the first study to describe maternal serum lactate concentrations in clinical chorioamnionitis at term. Physiologic inflammation during labor is not associated with changes in the maternal plasma lactate concentrations. However, pathologic inflammation as the one observed in patients with proven intra-amniotic infection is characterized by changes in the maternal serum lactate concentrations. (Figure Presented).

Database: EMBASE

13. Normal-range blood lactate concentration in septic shock is prognostic and predictive.

Author(s): Wacharasint, Petch; Nakada, Taka-aki; Boyd, John H; Russell, James A; Walley, Keith R

Source: Shock (Augusta, Ga.); Jul 2012; vol. 38 (no. 1); p. 4-10

Publication Date: Jul 2012

Publication Type(s): Research Support, Non-u.s. Gov't Randomized Controlled Trial Multicenter Study Journal Article

PubMedID: 22552014

Available in full text at [Shock](#) - from Ovid

Abstract: We hypothesized that lactate levels even within the normal range are prognostic and that low lactate levels predict a beneficial response to vasopressin infusion in septic shock. We conducted a retrospective analysis using the Vasopressin in Septic Shock Trial (VASST) as a derivation cohort (n = 665), then validated using another single-center septic shock cohort, St Paul's Hospital (SPH) cohort (n = 469). Lactate levels were divided into quartiles. The primary outcome variable was 28-day mortality in both cohorts. We used receiver operating characteristic (ROC) curve analysis to compare the prognostic value of lactate concentrations versus Acute Physiology and Chronic Health Evaluation II scores. We then explored whether lactate concentrations might predict beneficial response to vasopressin compared with noradrenaline in VASST. Normal lactate range is less than 2.3 mmol/L. At enrollment, patients in the second quartile ($1.4 < \text{lactate} < 2.3$ mmol/L) had significantly increased mortality and organ dysfunction compared with patients who had lactate ≤ 1.4 mmol/L (quartile 1) ($P < 0.0001$). Quartile 2 outcomes were as severe as quartile 3 ($2.3 \leq \text{lactate} < 4.4$ mmol/L) outcomes. Baseline lactate values (area under the ROC curve = 0.63, 0.66; VASST, SPH) were as good as Acute Physiology and Chronic Health Evaluation II scores (area under the ROC curve = 0.66, 0.73; VASST, SPH) as prognostic indicators of 28-day mortality. Lactate concentrations of 1.4 mmol/L or less predicted a beneficial response in those randomized to vasopressin compared with noradrenaline in VASST ($P < 0.05$). Lactate concentrations within the "normal" range can be a useful prognostic indicator in septic shock. Furthermore, patients whose lactate level is less than or equal to 1.4 mmol/L may benefit from vasopressin infusion.

Database: Medline

14. Early lactate levels for prediction of mortality in patients with sepsis or septic shock: A meta-analysis

Author(s): Liu G.; Lv H.; An Y.; Wei X.; Yi X.; Yi H.

Source: International Journal of Clinical and Experimental Medicine; Jan 2017; vol. 10 (no. 1); p. 37-47

Publication Date: Jan 2017

Publication Type(s): Review

Available in full text at [International Journal of Clinical and Experimental Medicine](#) - from Free Access Content

Abstract: Purpose: Early verification of septic patients at a higher risk of death is still a challenge. There exist several controversies that lactate measurement in septic patients predicted mortality. The present study aimed to explore the diagnostic accuracy of elevated early lactate levels in predicting mortality in septic or septic shock patients. Methods: Three databases including PubMed, Embase and the Cochrane Library were searched from inception to February 2016. We comprehensively performed a systematic review and meta-analysis of all prospective observational studies (POSs) and retrospective observational studies (ROSs) prognosticating mortality. Results: Eight prospective observational studies (POSs) and fourteen retrospective observational studies (ROSs) including a total of 28429 patients were identified. Elevated early lactate levels were significantly associated with increased risk of mortality (odds ratio (OR) 2.92, 95% confidence interval (CI) 2.40 to 3.55, $P < 0.00001$). The association was consistent for cut-off point of about 2 mmol/L (OR 3.21, 95% CI 2.07 to 4.97, $P < 0.00001$) and cut-off point of 4 mmol/L (OR 2.79, 95% CI 2.24 to 3.47, $P < 0.0001$). The overall sensitivity and specificity were 0.56 (95% CI, 0.48-0.64) and 0.70 (95% CI, 0.64-0.75), respectively. Conclusions: Our study demonstrates that an elevated initial lactate level may prove to be a powerful predictor of mortality in septic patients, and its prognostic performance is optimal for clinical utility. Future larger and more adequately powered prospective studies are awaited to clarify the optimal cut-off and the prognostic value of lactate in conjunction with other biomarkers. Copyright © 2017, E-Century Publishing Corporation. All rights reserved.

Database: EMBASE

15. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).

Author(s): Singer, Mervyn; Deutschman, Clifford S; Seymour, Christopher Warren; Shankar-Hari, Manu; Annane, Djillali; Bauer, Michael; Bellomo, Rinaldo; Bernard, Gordon R; Chiche, Jean-Daniel; Coopersmith, Craig M; Hotchkiss, Richard S; Levy, Mitchell M; Marshall, John C; Martin, Greg S; Opal, Steven M; Rubenfeld, Gordon D; van der Poll, Tom; Vincent, Jean-Louis; Angus, Derek C

Source: JAMA; Feb 2016; vol. 315 (no. 8); p. 801-810

Publication Date: Feb 2016

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Consensus Development Conference

PubMedID: 26903338

Available in print at [Patricia Bowen Library and Knowledge Service West Middlesex university Hospital](#) - from Journal of the American Medical Association (JAMA)

Abstract: IMPORTANCE Definitions of sepsis and septic shock were last revised in 2001. Considerable advances have since been made into the pathobiology (changes in organ function, morphology, cell biology, biochemistry, immunology, and circulation), management, and epidemiology of sepsis, suggesting the need for reexamination. OBJECTIVE To evaluate and, as needed, update definitions for sepsis and septic shock. PROCESS A task force (n = 19) with expertise in sepsis pathobiology, clinical trials, and epidemiology was convened by the Society of Critical Care Medicine and the European

Society of Intensive Care Medicine. Definitions and clinical criteria were generated through meetings, Delphi processes, analysis of electronic health record databases, and voting, followed by circulation to international professional societies, requesting peer review and endorsement (by 31 societies listed in the Acknowledgment).

KEY FINDINGS FROM EVIDENCE SYNTHESIS Limitations of previous definitions included an excessive focus on inflammation, the misleading model that sepsis follows a continuum through severe sepsis to shock, and inadequate specificity and sensitivity of the systemic inflammatory response syndrome (SIRS) criteria. Multiple definitions and terminologies are currently in use for sepsis, septic shock, and organ dysfunction, leading to discrepancies in reported incidence and observed mortality. The task force concluded the term severe sepsis was redundant.

RECOMMENDATIONS Sepsis should be defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. For clinical operationalization, organ dysfunction can be represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more, which is associated with an in-hospital mortality greater than 10%. Septic shock should be defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia. This combination is associated with hospital mortality rates greater than 40%. 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 a new bedside clinical score termed quickSOFA (qSOFA): respiratory rate of 22/min or greater, altered mentation, or systolic blood pressure of 100 mm Hg or less.

CONCLUSIONS AND RELEVANCE These updated definitions and clinical criteria should replace previous definitions, offer greater consistency for epidemiologic studies and clinical trials, and facilitate earlier recognition and more timely management of patients with sepsis or at risk of developing sepsis.

Database: Medline

16. Hyperlactatemia is an independent predictor of mortality and denotes distinct subtypes of severe sepsis and septic shock.

Author(s): Thomas-Rueddel, Daniel O; Poidinger, Bernhard; Weiss, Manfred; Bach, Friedhelm; Dey, Karin; Häberle, Helene; Kaisers, Udo; Rüddel, Hendrik; Schädler, Dirk; Scheer, Christian; Schreiber, Torsten; Schürholz, Tobias; Simon, Philipp; Sommerer, Armin; Schwarzkopf, Daniel; Weyland, Andreas; Wöbker, Gabriele; Reinhart, Konrad; Bloos, Frank; Medical Education for Sepsis Source Control and Antibiotics Study Group

Source: Journal of critical care; Apr 2015; vol. 30 (no. 2); p. 439

Publication Date: Apr 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Observational Study

PubMedID: 25466313

Available in full text at [Journal of Critical Care](#) - from ProQuest

Abstract: PURPOSE Current guidelines and most trials do not consider elevated lactate (Lac) serum concentrations when grading sepsis severity. We therefore assessed the association of different types of circulatory dysfunction regarding presence of hyperlactatemia and need for vasopressor support with clinical presentation and outcome of sepsis. METHODS In a secondary analysis of a prospective observational multicenter cohort study, 988 patients with severe sepsis were investigated regarding vasopressor support, Lac levels, and outcome. RESULTS Twenty-eight-day mortality regarding shock or hyperlactatemia was as follows: hyperlactatemia more than 2.5 mmol/L and septic shock (tissue dysoxic shock): 451 patients with a mortality of 44.8%; hyperlactatemia without vasopressor need (cryptic shock): 72 patients, mortality 35.3%; no hyperlactatemia with vasopressor need (vasoplegic shock): 331 patients, mortality 27.7%; and absence of hyperlactatemia or overt shock (severe sepsis): 134 patients, mortality 14.2% (P 4 mmol/L) was independent of vasopressor support (P 0.1 µg/kg per minute) in logistic regression. CONCLUSIONS Hyperlactatemia increases risk of death independent of vasopressor need resulting in different phenotypes within the classic categories of severe sepsis and septic shock.

Database: Medline

17. Lactate measurements in sepsis-induced tissue hypoperfusion: Results from the surviving sepsis campaign database

Author(s): Casserly B.; Levy M.M.; Selvakumar N.; Phillips G.S.; Schorr C.; Dellinger R.P.; Townsend S.R.; Osborn T.M.; Reinhart K.

Source: Critical Care Medicine; Mar 2015; vol. 43 (no. 3); p. 567-573

Publication Date: Mar 2015

Publication Type(s): Article

PubMedID: 25479113

Available in full text at [Critical Care Medicine](#) - from Ovid

Abstract: Objective: The Surviving Sepsis Campaign guidelines recommend obtaining a serum lactate measurement within 6 hours of presentation for all patients with suspected severe sepsis or septic shock. A lactate greater than 4 mmol/L qualifies for administration of early quantitative resuscitation therapy. We evaluated lactate elevation (with special attention to values > 4 mmol/L) and presence or absence of hypotension as a marker of clinical outcome. Design and Setting: The Surviving Sepsis Campaign developed a database to assess the overall effect of the sepsis bundles as a performance improvement tool for clinical practice and patient outcome. This analysis focuses on one element of the Surviving Sepsis Campaign's resuscitation bundle, measuring serum lactate in adult severe sepsis or septic shock patients and its interaction with hypotension. This analysis was conducted on data

submitted from January 2005 through March 2010. Subjects: Data from 28,150 subjects at 218 sites were analyzed. Interventions: None. Measurements and Main Results: Unadjusted analysis of the 28,150 observations from the Surviving Sepsis Campaign database demonstrated a significant mortality increase with the presence of hypotension in conjunction with serum lactate elevation greater than 2 mmol/L. On multivariable analysis, only lactate values greater than 4 mmol/L, in conjunction with hypotension, significantly increased mortality when compared with the referent group of lactate values less than 2 mmol/L and not hypotensive. Mortality was 44.5% in patients with combined lactate greater than 4 mmol/L and hypotension when compared with 29% mortality in patients not meeting either criteria. Conclusions: Serum lactate was commonly measured within 6 hours of presentation in the management of severe sepsis or septic shock in this subset analysis of the Surviving Sepsis Campaign database in accordance with the Surviving Sepsis Campaign guidelines. Our results demonstrate that elevated lactate levels are highly associated with in-hospital mortality. However, only patients who presented with lactate values greater than 4 mmol/L, with and without hypotension, are significantly associated with in-hospital mortality and is associated with a significantly higher risk than intermediate levels (2-3 and 3-4 mmol/L). This supports the use of the cutoff of greater than 4 mmol/L as a qualifier for future clinical trials in severe sepsis or septic shock in patient populations who use quantitative resuscitation and the Surviving Sepsis Campaign bundles as standard of care. Copyright © 2015 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

Database: EMBASE

18. Sepsis-associated hyperlactatemia.

Author(s): Garcia-Alvarez, Mercedes; Marik, Paul; Bellomo, Rinaldo

Source: Critical care (London, England); Sep 2014; vol. 18 (no. 5); p. 503

Publication Date: Sep 2014

Publication Type(s): Journal Article Review

PubMedID: 25394679

Available in full text at [Critical Care](#) - from Free Access Content

Available in full text at [Critical Care](#) - from National Library of Medicine

Abstract: There is overwhelming evidence that sepsis and septic shock are associated with hyperlactatemia (sepsis-associated hyperlactatemia (SAHL)). SAHL is a strong independent predictor of mortality and its presence and progression are widely appreciated by clinicians to define a very high-risk population. Until recently, the dominant paradigm has been that SAHL is a marker of tissue hypoxia. Accordingly, SAHL has been interpreted to indicate the presence of an 'oxygen debt' or 'hypoperfusion', which leads to increased lactate generation via anaerobic glycolysis. In light of such interpretation of the meaning of SAHL, maneuvers to increase oxygen delivery have been proposed as its treatment. Moreover, lactate levels have been proposed as a method to evaluate the adequacy of resuscitation and the nature of the response to the initial treatment for sepsis. However, a large body of evidence has accumulated that strongly challenges such notions. Much evidence now supports the view that SAHL is not due only to tissue hypoxia or anaerobic glycolysis. Experimental and human studies all consistently support the view that SAHL is more logically explained by increased aerobic glycolysis secondary to activation of the stress response (adrenergic stimulation). More importantly, new evidence suggests that SAHL may actually serve to facilitate bioenergetic efficiency through an increase in lactate oxidation. In this sense, the characteristics of lactate production best fit the notion of an adaptive survival response that grows in intensity as disease severity increases. Clinicians need to be aware of these developments in our understanding of SAHL in order to approach patient management according to biological principles and to interpret lactate concentrations during sepsis resuscitation according to current best knowledge.

Database: Medline

19. Lactic acid measurement to identify risk of morbidity in pregnancy

Author(s): Albright C.; Lopes V.; Rouse D.; Anderson B.; Ali T.

Source: American Journal of Obstetrics and Gynecology; Jan 2014; vol. 210 (no. 1)

Publication Date: Jan 2014

Publication Type(s): Conference Abstract

Abstract:OBJECTIVE: Lactic acid (LA) is a well-known marker for sepsis. The utility of LA measurement for sepsis in pregnancy is unknown and is the objective of this study. STUDY DESIGN: Retrospective cohort of pregnant and postpartum patients with clinical suspicion of sepsis in the ED. Data abstracted included temperature, heart rate, blood pressure, respiratory rate, oxygen saturation, white blood cell count, percentage of immature neutrophils, and LA. Outcomes included intensive care unit (ICU) admission, telemetry unit admission, positive blood cultures, positive influenza swabs, and perinatal outcome. A linear regression model was used to evaluate the association between LA and adverse outcome. Outcomes were also compared by mean LA level. RESULTS: Of 850 eligible women included, 159 had LA drawn. LA level was positively associated with requiring a higher level of care (admission to an ICU or telemetry unit), adjusted odds ratio (AOR) 2.34, 95% confidence interval (CI), 1.33-4.12, and positive blood cultures (AOR 1.6, 95% CI 0.83-3.08). In patients admitted to the ICU, the mean LA level was 2.6, versus 1.6 in those not admitted to the ICU, $p=0.04$. A similar trend was seen in those requiring telemetry unit admission (2.0 versus 1.6, $p=0.03$) and with positive blood cultures (2.2 versus 1.6, $p=0.003$). Patients who had LA drawn differed from those who did not. Overall, they had higher morbidity rates: more likely to have positive blood cultures (16.8 versus 5.5%, $p=0.039$), require ICU (5 versus 0.1%, $p<0.0001$) or telemetry unit (17.2 versus 0.9%) admission, have a longer hospital stay (3.5 versus 2.7 days, $p=0.0002$), and deliver preterm (18.3 versus 10.9%, $p=0.049$). There was no association, nor was there a difference in the LA level, among patients with positive influenza swabs or in perinatal outcome. CONCLUSION: Elevated LA in pregnancy is associated with adverse outcomes from sepsis, including increased risk of ICU and telemetry unit admission and positive blood cultures. In this cohort, having LA drawn was a marker of more severe infection.

Database: EMBASE

20. Reclassifying the spectrum of septic patients using lactate: severe sepsis, cryptic shock, vasoplegic shock and dysoxic shock.

Author(s): Ranzani, Otavio Tavares; Monteiro, Mariana Barbosa; Ferreira, Elaine Maria; Santos, Sergio Ricardo; Machado, Flavia Ribeiro; Noritomi, Danilo Teixeira; Grupo de Cuidados Críticos Amil

Source: Revista Brasileira de terapia intensiva; 2013; vol. 25 (no. 4); p. 270-278

Publication Date: 2013

Publication Type(s): Multicenter Study Journal Article Observational Study

PubMedID: 24553507

Available in full text at [Revista Brasileira de Terapia Intensiva](#) - from National Library of Medicine

Abstract:OBJECTIVEThe current definition of severe sepsis and septic shock includes a heterogeneous profile of patients. Although the prognostic value of hyperlactatemia is well established, hyperlactatemia is observed in patients with and without shock. The present study aimed to compare the prognosis of septic patients by stratifying them according to two factors: hyperlactatemia and persistent hypotension.METHODThe present study is a secondary analysis of an observational study conducted in ten hospitals in Brazil (Rede Amil - SP). Septic patients with initial lactate measurements in the first 6 hours of diagnosis were included and divided into 4 groups according to hyperlactatemia (lactate >4mmol/L) and persistent hypotension: (1) severe sepsis (without both criteria); (2) cryptic shock (hyperlactatemia without persistent hypotension); (3) vasoplegic shock (persistent hypotension without hyperlactatemia); and (4) dysoxic shock (both criteria).RESULTSIn total, 1,948 patients were analyzed, and the sepsis group represented 52% of the patients, followed by 28% with vasoplegic shock, 12% with dysoxic shock and 8% with cryptic shock. Survival at 28 days differed among the groups ($p<0.001$). Survival was highest among the severe sepsis group (69%, $p<0.001$ versus others), similar in the cryptic and vasoplegic shock groups (53%, $p=0.39$), and lowest in the dysoxic shock group (38%, $p<0.001$ versus others). In the adjusted analysis, the survival at 28 days remained different among the groups ($p<0.001$) and the dysoxic shock group exhibited the highest hazard ratio (HR=2.99, 95%CI 2.21-4.05).CONCLUSIONThe definition of sepsis includes four different profiles if we consider the presence of hyperlactatemia. Further studies are needed to better characterize septic patients, to understand the etiology and to design adequate targeted treatments.

Database: Medline

21. Mild elevation in serum lactate < 4 mmol/dl is associated with mortality in critically ill patients with severe sepsis and septic shock

Author(s): Lanspa M.J.; Dickerson J.; Brown S.M.; Knox D.B.

Source: American Journal of Respiratory and Critical Care Medicine; 2013; vol. 187

Publication Date: 2013

Publication Type(s): Conference Abstract

Available in full text at [American Journal of Respiratory and Critical Care Medicine](#) - from ProQuest

Available in full text at [American Journal of Respiratory and Critical Care Medicine](#) - from Free Access Content

Abstract:Rationale: Elevations in serum lactate may correlate with high mortality in patients with septic shock, but it is unknown if mild elevation of lactate (< 4 mmol/dL) has any clinical significance. Methods: Using the highly detailed electronic medical record of Intermountain Healthcare, we analyzed patients treated with a severe sepsis and septic shock bundle of care process at Intermountain hospital intensive care units from 2004 to 2010. We analyzed all patients who had an APACHE II score and serum lactate obtained upon admission to an intensive care unit. We performed multivariate logistic regression for inpatient mortality with covariates of age, Charlson comorbidity index, modified APACHE II score (omitting age and medical comorbidity components), and lactate. Results: We evaluated 4,591 patients from 12 hospitals. APACHE II scores were calculated in 2,058 patients, of whom 1,436 had an initial serum lactate < 4 mmol/dL. Medians [with interquartile ranges] were calculated for age (62, 51-74), modified APACHE II score (17, 12-23), and Charlson comorbidity index (4, 2-7). After controlling for age, modified APACHE II, and Charlson comorbidity index using multivariate logistic regression, serum lactate was associated with mortality in patients with severe sepsis or septic shock and a lactate < 4 mmol/dL (odds ratio 1.24, p = 0.04). Area under the curve of the model was 0.77. Conclusion: Mild elevation of serum lactate (< 4 mmol/dL) was associated with increased odds of mortality among patients admitted to an intensive care unit with severe sepsis and septic shock. Further investigation is warranted to determine if mild elevation in lactate may offer prognostic value. (Table Presented).

Database: EMBASE

22. Fluid volume, lactate values, and mortality in sepsis patients with intermediate lactate values

Author(s): Liu V.; Escobar G.J.; Morehouse J.W.; Soule J.; Whippy A.

Source: Annals of the American Thoracic Society; Oct 2013; vol. 10 (no. 5); p. 466-473

Publication Date: Oct 2013

Publication Type(s): Article

PubMedID: 24004068

Available in full text at [Annals of the American Thoracic Society](#) - from ProQuest

Abstract:Rationale: Patients with severe sepsis without shock or tissue hypoperfusion face substantial mortality; however, treatment guidelines are lacking. Objectives: To evaluate the association between intravenous fluid resuscitation, lactate clearance, and mortality in patients with "intermediate" lactate values of 2 mmol/L or greater and less than 4 mmol/L. Measurements and Main Results: This was a retrospective study of 9,190 patients with sepsis with intermediate lactate values. Interval changes between index lactate values and those at 4, 8, and 12 hours were calculated with corresponding weight-based fluid volumes. Outcomes included lactate change and mortality. Repeat lactate tests were completed in 94.7% of patients within 12 hours. Hospital and 30-day mortality were 8.2 and 13.3%, respectively, for patients with lactate clearance; they were 18.7 and 24.7%, respectively, for those without lactate clearance. Each 10% increase in repeat

lactate values was associated with a 9.4% (95% confidence interval [CI] = 7.8-11.1%) increase in the odds of hospital death. Within 4 hours, patients received 32 (618) ml/kg of fluid. Each 7.5 ml/kg increase was associated with a 1.3% (95% CI = 0.6-2.1%) decrease in repeat lactate. Across an unrestricted range, increased fluid was not associated with improved mortality. However, when limited to less than 45 ml/kg, additional fluid was associated with a trend toward improved survival (odds ratio = 0.92; 95% CI = 0.82- 1.03) that was statistically significant among patients with highly concordant fluid records. Conclusions: Early fluid administration, below 45 ml/kg, was associated with modest improvements in lactate clearance and potential improvements in mortality. Further study is needed to define treatment strategies in this prevalent and morbid group of patients with sepsis. Copyright © 2013 by the American Thoracic Society.

Database: EMBASE

23. Early lactate clearance in septic patients with elevated lactate levels admitted from the emergency department to intensive care: Time to aim higher?

Author(s): Walker C.A.; Griffith D.M.; Gray A.J.; Datta D.; Hay A.W.

Source: Journal of Critical Care; Oct 2013; vol. 28 (no. 5); p. 832-837

Publication Date: Oct 2013

Publication Type(s): Article

PubMedID: 23602032

Available in full text at [Journal of Critical Care](#) - from ProQuest

Abstract: Purpose: Septic patients with hyperlactatemia have increased mortality rates, irrespective of hemodynamic and oxygen-derived variables. The aims of the study are the following: (1) to ascertain whether lactate clearance (LC) (percentage change in lactate over unit time) predicts mortality in septic patients admitted to intensive care directly from the emergency department and (2) to calculate the optimal "cut-off" value for mortality prediction. Methods: Three-year retrospective observational study of consecutive patients with severe sepsis and septic shock admitted to intensive care from the emergency department of a tertiary UK hospital. We calculated 6-hour LC, performed receiver operating characteristic analyses to calculate optimal cut-off values for initial lactate and LC, dichotomized patients according to the LC cut-off, and calculated hazard ratios using a Cox proportional hazards model. Results: One hundred six patients were identified; 78, after exclusions. Lactate clearance was independently associated with 30-day mortality ($P < .04$); optimal cut-off, 36%. Mortality rates were 61.1% and 10.7% for patients with 6-hour LC 36% or less and greater than 36%, respectively. Hazard ratio for death with LC 36% or less was 7.33 (95% confidence interval, 2.17-24.73; $P < .001$). Conclusions: Six-hour LC was independently associated with mortality, and the optimal cut-off value was 36%, significantly higher than previously reported. We would support further research investigating this higher LC as a distinct resuscitation end point in patients with severe sepsis and septic shock. © 2013 Elsevier Inc.

Database: EMBASE

24. Predicting factors associated with clinical deterioration of sepsis patients with intermediate levels of serum lactate.

Author(s): Song, Young Hoon; Shin, Tae Gun; Kang, Mun Ju; Sim, Min Seob; Jo, Ik Joon; Song, Keun Jeong; Jeong, Yeon Kwon

Source: Shock (Augusta, Ga.); Aug 2012; vol. 38 (no. 3); p. 249-254

Publication Date: Aug 2012

Publication Type(s): Journal Article

PubMedID: 22683735

Available in full text at [Shock](#) - from Ovid

Abstract: Clinical deterioration among hemodynamically stable sepsis patients occurs frequently, and patients with intermediate lactate levels (between 2.0 and 4.0 mmol/L) are particularly at risk for mortality. The aim of this study was to identify factors for predicting early deterioration in sepsis patients with intermediate levels of serum lactate. A retrospective cohort study of adult sepsis patients with lactate levels between 2.0 and 4.0 mmol/L was conducted in the emergency department of a tertiary care hospital between August 2008 and July 2010. The primary outcome was progression to sepsis-induced shock defined as persistent hypotension despite initial fluid challenge or a blood lactate concentration 4 mmol/L or greater within 72 hours of emergency department arrival. Among the 474 patients enrolled in the study, there were 108 cases of sepsis-induced tissue hypoperfusion (22.7%) and 48 deaths (10.1%). In a multivariate regression analysis, independent predictors for progression were hyperthermia, neutropenia, band neutrophils appearance, hyponatremia, blood urea nitrogen level, serum lactate level, and organ failure including respiratory, cardiovascular, and central nervous system. Initial Sequential Organ Failure Assessment score was also associated with progression. In patients with a Sequential Organ Failure Assessment score of 5 or greater, the predicted rate of progression to tissue hypoperfusion was 38.9%. Our study demonstrates potential risk factors, including organ failure, for progression to sepsis-induced tissue hypoperfusion in patients with intermediate levels of serum lactate. We suggest that an early aggressive treatment strategy is needed in patients with these risk factors.

Database: Medline

25. Serum level of lactate dehydrogenase, homocystein, hemoglobin and platelet in preeclampsia

Author(s): Borghei A.; Nosrat B.S.; Ghaemi E.; Azarhoosh R.; Besharat S.; Sedaghati M.

Source: Pakistan Journal of Medical Sciences; 2011; vol. 27 (no. 5); p. 1014-1017

Publication Date: 2011

Publication Type(s): Article

Available in full text at [Pakistan Journal of Medical Sciences](#) - from Free Access Content

Abstract: Objectives: Pre-eclampsia affects approximately 5-8% of pregnant women. The aim of this study was to compare the serum level of Lactate dehydrogenase (LDH), Homocystein, Hemoglobin and platelet in pregnant women diagnosed as pre-eclampsia and a normal group in Gorgan city, Northeastern Iran from 2007-2008. Methodology: In this case control study, 50 cases of pre-eclampsia were compared with the control group women hospitalized in Dezyani hospital. Pre-eclampsia criteria were: Blood pressure more than or equal to 140/90 mm hg and Proteinuria greater or equal to 300 mg/ 24 hours urine sample in the third trimester. Hemoglobin, platelet, LDH and homocystein were measured. Data were analyzed by the mean of SPSS-14 program & Chi-2 or t-student were used. Results: The difference of BMI and family incomes was significant between two groups (P-value 0.01). Homocystein level was more than normal range in five patients with pre-

eclampsia (P-value<0.001). Conclusions: In this study, homocystein level was significantly higher in pre-eclampsia patients but LDH, hemoglobin and platelet level had no significant difference.

Database: EMBASE

26. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock.

Author(s): Mikkelsen, Mark E; Miltiades, Andrea N; Gaieski, David F; Goyal, Munish; Fuchs, Barry D; Shah, Chirag V; Bellamy, Scarlett L; Christie, Jason D

Source: Critical care medicine; May 2009; vol. 37 (no. 5); p. 1670-1677

Publication Date: May 2009

Publication Type(s): Research Support, N.i.h., Extramural Comparative Study Journal Article

PubMedID: 19325467

Available in full text at [Critical Care Medicine](#) - from Ovid

Abstract:PRINCIPLESerum lactate is a potentially useful biomarker to risk-stratify patients with severe sepsis; however, it is plausible that elevated serum lactate is simply a manifestation of clinically apparent organ dysfunction and/or shock (i.e., refractory hypotension).OBJECTIVETo test whether the association between initial serum lactate level and mortality in patients presenting to the emergency department (ED) with severe sepsis is independent of organ dysfunction and shock.DESIGNSingle-center cohort study. The primary outcome was 28-day mortality and the risk factor variable was initial venous lactate (mmol/L), categorized as low (or = 4). Potential covariates included age, sex, race, acute and chronic organ dysfunction, severity of illness, and initiation of early goal-directed therapy. Multivariable logistic regression analyses were stratified on the presence or absence of shock.SETTINGThe ED of an academic tertiary care center from 2005 to 2007.PATIENTSEight hundred thirty adults admitted with severe sepsis in the ED.INTERVENTIONSNone.MEASUREMENTS AND MAIN RESULTSMortality at 28 days was 22.9% and median serum lactate was 2.9 mmol/L. Intermediate (odds ratio [OR] = 2.05, p = 0.024) and high serum lactate levels (OR = 4.87, p < 0.001) were associated with mortality in the nonshock subgroup. In the shock subgroup, intermediate (OR = 3.27, p = 0.022) and high serum lactate levels (OR = 4.87, p = 0.001) were also associated with mortality. After adjusting for potential confounders, intermediate and high serum lactate levels remained significantly associated with mortality within shock and nonshock strata.CONCLUSIONSInitial serum lactate was associated with mortality independent of clinically apparent organ dysfunction and shock in patients admitted to the ED with severe sepsis. Both intermediate and high serum lactate levels were independently associated with mortality.

Database: Medline

27. Serum lactate as a predictor of mortality in patients with infection.

Author(s): Trzeciak, Stephen; Dellinger, R Phillip; Chansky, Michael E; Arnold, Ryan C; Schorr, Christa; Milcarek, Barry; Hollenberg, Steven M; Parrillo, Joseph E

Source: Intensive care medicine; Jun 2007; vol. 33 (no. 6); p. 970-977

Publication Date: Jun 2007

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 17431582

Available in full text at [Intensive Care Medicine](#) - from ProQuest

Available in full text at [Intensive Care Medicine](#) - from Springer Link Journals

Abstract:OBJECTIVETo determine the utility of an initial serum lactate measurement for identifying high risk of death in patients with infection.DESIGN AND SETTINGPost-hoc analysis of a prospectively compiled registry in an urban academic hospital.PARTICIPANTSPatients with (a) a primary or secondary diagnosis of infection and (b) lactate measurement who were admitted over the 18 months following hospital-wide implementation of the Surviving Sepsis Campaign guideline for lactate measurement in patients with infection and possible severe sepsis. There were 1,177 unique patients, with an in-hospital mortality of 19%.MEASUREMENTS AND RESULTSOutcome measures included acute-phase (≥ 4.0 mmol/l and performed a Bayesian analysis to determine its impact on a full range (0.01-0.99) of hypothetical pretest probability estimates for death. In-hospital mortality was 15%, 25%, and 38% in low, intermediate, and high lactate groups, respectively. Acute-phase deaths and in-hospital deaths increased linearly with lactate. An initial lactate ≥ 4.0 mmol/l was associated with sixfold higher odds of acute-phase death; however, a lactate level less than 4 mmol/l had little impact on probability of death.CONCLUSIONSWhen broadly implemented in routine practice, measurement of lactate in patients with infection and possible sepsis can affect assessment of mortality risk. Specifically, an initial lactate ≥ 4.0 mmol/l substantially increases the probability of acute-phase death.

Database: Medline

Strategy 254070

#	Database	Search term	Results
1	Medline	(lactate OR lactic).ti,ab	125302
2	Medline	exp "LACTIC ACID"/	37919
3	Medline	(1 OR 2)	135988
4	Medline	(labor OR labour OR cesarean* OR caesarean* OR "c section").ti,ab	125743
6	Medline	exp "CESAREAN SECTION"/	39757
7	Medline	("labor obstetric").af	28119
8	Medline	(4 OR 6 OR 7)	149166
9	Medline	(sepsis OR septic*).ti,ab	126340
10	Medline	exp SEPSIS/	107128
11	Medline	(9 OR 10)	185125
12	Medline	(3 AND 8 AND 11)	5
13	Medline	(3 AND 8)	642
14	Medline	(3 AND 11)	3138
15	Medline	(pregn* OR obstetric*).ti,ab	457128
16	Medline	exp PREGNANCY/	813274
17	Medline	(15 OR 16)	923170
18	Medline	(3 AND 11 AND 17)	51
19	Medline	exp HYPERLACTATEMIA/	63
20	Medline	(8 AND 19)	0

21	Medline	(11 AND 19)	14
22	Medline	(level* OR concentration*).ti	443199
23	Medline	(14 AND 22)	186
24	Medline	exp "REFERENCE VALUES"/	151688
25	Medline	(14 AND 24)	41
26	Medline	(3 AND 8 AND 24)	14
27	Medline	(3 AND 17 AND 24)	59
28	EMBASE	*"LACTATE BLOOD LEVEL"/ OR *"LACTATE DEHYDROGENASE BLOOD LEVEL"/	2698
29	EMBASE	exp "REFERENCE VALUE"/	119597
30	EMBASE	(28 AND 29)	84
31	EMBASE	exp PREGNANCY/	672177
32	EMBASE	exp LABOR/	35785
33	EMBASE	(31 OR 32)	686132
34	EMBASE	(28 AND 33)	50
35	EMBASE	exp SEPSIS/	220270
36	EMBASE	(28 AND 35)	193
37	EMBASE	exp "LACTATE BLOOD LEVEL"/	15427
38	EMBASE	(33 AND 35 AND 37)	24
39	EMBASE	(bundle).ti,ab	44079
40	EMBASE	(28 AND 39)	5

41	EMBASE	(lactate OR lactic).ti	33881
42	EMBASE	(33 AND 41)	572
43	EMBASE	(35 AND 42)	9
44	EMBASE	(cutoff OR "cut off").ti,ab	77690
45	EMBASE	(28 AND 44)	59
46	Medline	(cutoff OR "cut off").ti,ab	43286
47	Medline	(3 AND 46)	412
48	Medline	exp BIOMARKERS/	787776
49	Medline	(3 AND 11 AND 48)	307
50	Medline	(lactate ADJ2 4).ti,ab	1543
51	Medline	(11 AND 50)	147
52	EMBASE	(lactate ADJ2 4).ti,ab	684
53	EMBASE	(35 AND 52)	184
54	EMBASE	(28 AND 52)	31
55	EMBASE	*HYPERLACTATEMIA/	494
56	EMBASE	(33 AND 55)	7
57	EMBASE	(29 AND 33 AND 37)	9
58	EMBASE	(29 AND 33 AND 37)	9
59	EMBASE	exp "LACTIC ACID"/	62371
60	EMBASE	(29 AND 33 AND 59)	25
61	EMBASE	(33 AND 35 AND 59)	31
62	Medline	(normal* ADJ2 lactate*).ti,ab	1024

63	Medline	(17 AND 62)	46
64	EMBASE	(normal* ADJ2 lactate*).ti,ab	1013
65	EMBASE	exp "NORMAL VALUE"/	57595
66	EMBASE	(28 AND 65)	47
67	EMBASE	(64 OR 66)	1060
68	EMBASE	(33 AND 67)	38
69	EMBASE	(28 AND 65)	47
70	EMBASE	(elevat*).ti,ab	836177
71	EMBASE	(28 AND 33 AND 70)	9
72	EMBASE	(obstetric*).ti,ab	117898
73	EMBASE	(28 AND 70 AND 72)	3
74	EMBASE	(elevat* ADJ3 lactate).ti,ab	4439
75	EMBASE	(33 AND 74)	73
76	Medline	(elevat* ADJ3 lactate).ti,ab	3681
77	Medline	(8 AND 76)	14
78	EMBASE	exp "CESAREAN SECTION"/	80836
79	EMBASE	(28 AND 78)	14