Research Article

Serum lactate: an independent predictor of severe sepsis in obstetric patients

Alveera[*], Prema D' Cunha[**]

[*]Resident, [**]Professor and H.O.D; Department of Obstetrics and Gynecology, Father Muller Medical College, Father Muller Road, Mangalore, Karnataka – 575002 INDIA.
Email: alveerads@gmail.com

Abstract

Objectives: to determine the utility of serum lactate as an effective and independent indicator of severe sepsis in patients with obstetric related sepsis. **Methods:** the study was conducted on 40 patients admitted to our hospital on in patient basis with 2 or more signs and symptoms of infection, along with a suspected source of infection. Once sepsis was diagnosed, a baseline serum lactate was done in these patients and further evaluated over a period of time. **Results:** out of the 40 patients studied, it was found that not all patients with sepsis had an elevated serum lactate levels. During the study, it was found that patients with an initial raised lactate level (≥2.2mmol), needed more aggressive treatment and a closer follow up during their period of stay in the hospital. Although all patients with elevated serum lactate had severe sepsis, lactate was not the only determining factor, patients in whom other laboratory parameters were altered, and where lactate was normal were also found to be in severe sepsis. **Conclusion:** Serum lactate is an independent and effective predictor of obstetric related sepsis.

Keyword: Serum lactate, sepsis, obstetrics, prognosis.

[*]**Address for Correspondence:**
Dr. Alveera D' Souza, Resident, Department of Obstetrics and Gynecology, Father Muller Medical College, Father Muller Road, Mangalore, Karnataka – 575002 INDIA.
Email: alveerads@gmail.com
Received Date: 01/09/2014 Accepted Date: 01/09/2014

Access this article online	
Quick Response Code:	Website: www.statperson.com
	DOI: ---

INTRODUCTION

Recent studies have proved that sepsis is one of the leading cause for maternal mortality. Many biomarkers including serum lactate has been well established in patients with suspected sepsis[1]. Serum lactate concentrations are already being used in most ICU's in order to monitor patients with sepsis. In addition blood lactate levels have been shown to have greater prognostic value than oxygen derived variables. Elevated serum lactate levels is known to have poor prognosis in patients with sepsis. The current guidelines as per the surviving sepsis campaign[2] advocate serum lactate measurement in all patients with suspected sepsis. Based on this guideline, serum lactate has been included as part of quality indicators for performance improvement in sepsis resuscitation. This is mainly intended in patients admitted with suspected sepsis in all hospital based settings and is usually elevated secondary to anaerobic metabolism due to hypoperfusion. Previously CRP[3] was used as a part of routine investigation in maternal infection. But its non-specific nature makes it less reliable to depend on. Although, it can be used along with blood lactate in the prognosis and assessment of mortality risk in patients with sepsis. Therefore the purpose of this study is to determine the utility of serum lactate as a prognostic tool in the identification of high risk of death in patients with sepsis and its effectiveness as an independent predictor of severe sepsis in patients with associated organ failure.

OBJECTIVES AND AIMS

To establish serum lactate as an independent and effective predictor of severe sepsis in patients with associated organ failure.

Methodology

Patient selection

This study was conducted in the Department of Obstetrics and Gynaecology, Father Muller medical college,

How to site this article: Alveera, Prema D' Cunha. Serum lactate: an independent predictor of severe sepsis in obstetric patients. *International Journal of Recent Trends in Science and Technology* November 2014; 13(1): 05-10 http://www.statperson.com (accessed 01 November 2014).

mangalore from august 2012 till July 2014. The study was a comparative study and data collected was analysed bymean, standard deviation, frequency, percentage, unpaired 't' test and by Chi square test. All patients satisfying the inclusion criteria were selected for the study after taking informed consent. Patients with exclusion criteria were excluded.

Inclusion criteria

All antenatal or postnatal mothers with primary or secondary diagnosis of sepsis. Patients with two or more signs and symptoms of infection such as Fever, tachycardia, tachypnea, hypotension, hyper/hypothermia, leucocytosis or altered mental status and at least 1 suspected source of infection such as mastitis, respiratory infections, cardiac dysfunction, cellulitis, fetal demise, unexplained fetal tachycardia, abdominal pain/distension, episiotomy or surgery site infection, urinary or catheter infections, IV line infection, neck stiffness with altered sensorium, PROM / PPROM or puerperal sepsis.

Exclusion criteria

Women reviewing on out-patient basis and women who are immuno-compromised.

A total of 40 patients who fulfilled the inclusion criteria were allocated into the study.

MATERIALS AND METHODS

Lactate is the end product of anaerobic glycolysis. Accumulation of lactate in blood is due to increased production and decreased removal by liver

PROCEDURE NAME

Spectrophotometric, kinetic, enzymatic

EXPLANATION OF TEST

Lactate measurements that evaluate the acid-base status are used in the diagnosis and treatment of lactic acidosis. Estimation of lactate in blood is used to detect lactic acidosis in persons with underlying risk factors such as cardiovascular or renal disease that predispose them to acid base imbalance. Lactate is elevated in a variety of conditions in which hypoxia occurs and in liver disease. Also it is significantly elevated in severe sepsis secondary to anaerobic metabolism.

CLINICAL IMPLICATIONS

Blood lactate levels are increased in ; lactic acidosis ; cardiac failure; pulmonary failure; haemorrhage; diabetes; shock; liver disease and severe sepsis.

PRINCIPLE OF THE METHOD

L-lactate is oxidized to pyruvate by the specific enzyme lactate oxidase (LOD). Peroxidase (POD) is used to generate a coloured dye using the hydrogen peroxide generated in the first reaction.

$$\text{L-lactate} + O_2 \xrightarrow{\text{LOD}} \text{pyruvate} + H_2O_2$$

$$2\,H_2O_2 + \text{H donor} + \text{4-AAP} \xrightarrow{\text{POD}} \text{chromogen} + 2\,H_2O$$

The intensity of the colour formed is directly proportional to the L-lactate concentration. It is determined by measuring the increase in absorbance.

SAMPLE COLLECTION

Patients admitted to the hospital on in patient basis with a suspicion of sepsis were thoroughly investigated and a baseline serum lactate was sent in ice packs to the biochemistry laboratory immediately. These lactate values were then repeated after 12hours and 24hours respectively in all patients with positive baseline values ($\geq$2.2mmol).

SPECIMEN TYPE, VOLUME, STABILITY, STORAGE AND PRECAUTIONS

Plasma: Na-fluoride/K-oxalate and Na-fluoride/Na-heparin plasma.

These samples were transported immediately in ice packs to the biochemistry lab.

Centrifuge within 15 minutes of collecting the specimen. Stability in plasma (separated): 8 hours at 15-25 °C; 14 days at 2-8 °C.

STORAGE AND REAGENT DETERIORATION

Reagents are stable for 12 weeks on board in use and refrigerated on the analyzer; exp. date on the pack was considered for use. Reagents were stored at 2-8^0 C

EQUIPMENT

Roche Hitachi Cobas 6000 fully automated analyzer.

PROCEDURE

Assay procedure: The primary tube or the sample transferred into a sample cup is loaded in the sample disc of the Roche Hitachi Cobas 6000 fully automated analyzer. Note the position of the sample on the sample disc. Selecting Stat/Routine type the sample ID and select the test Lactate. Main wavelength: 660 nm, sub 700 nm. Start the machine after checking that the start position number corresponds to the sample position. Refer kit insert.

CALIBRATIONS

Calibration is done with the C.F.A.S. A two-point Calibration is done following every reagent lot change; after maintenance and service of instrument, and as a part of quality control procedures.

REFERENCE VALUES

0.5-2.2 mmol/L

RESULTS

Table 1: Distribution of Age

	Frequency	Percent
25 and below	12	30.0
26-30	22	55.0
Above 30	6	15.0
Total	**40**	**100**

Table 1. Shows the age distribution of the patients included in the study. The commonest age group was between 26-30 years, as this is the commonest reproductive age in our hospital.

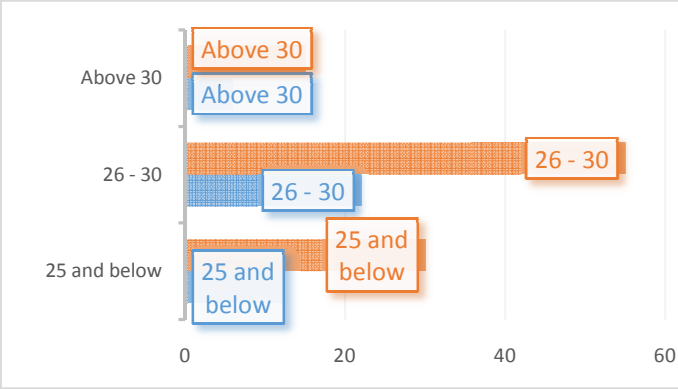

Figure 1: Shows the age distribution among the study patients

Table 2: Univariate analysis of age distribution

	N	Minimum	Maximum	Mean	SD
Age	40	23	36	27.20	3.406

Table 3: Distribution of Obstetric Score

	Frequency	Percent
Primigravida	11	27.5
Multigravida	29	72.5
Total	**40**	**100.0**

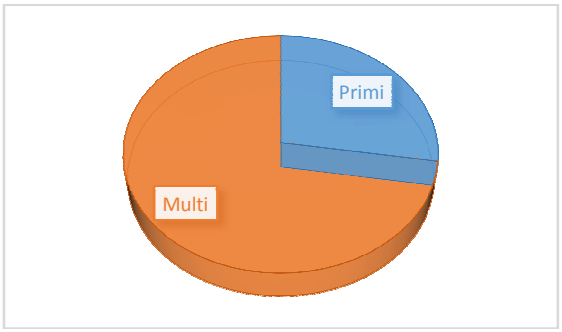

Figure 2: Shows the distributions of the period of gestation among the study patients

Shows the parity distribution among these patients, the most common being mutigravidas

Table 4: Distribution of gestation age

Antenatal	Frequency	Percentage
Less than 28 weeks	4	22.22
28 - 35 weeks	11	61.11
More than 35 weeks	3	16.67
Total	**18**	**100**
Post Natal	22	100

This table shows that the most common period of gestation in the antenatal patients with sepsis was between 28 – 35 weeks. But the postnatal mothers were the most vulnerable group.

Table 5: Distribution of Signs and Symptoms of Infection

	Frequency	Percentage
altered mental status	2	2.38
Fever	32	38.10
Hypotension	13	15.48
Leucocytosis	9	10.71
Tachycardia	22	26.19
Tachypnea	6	7.14
Total	**84**	**100**

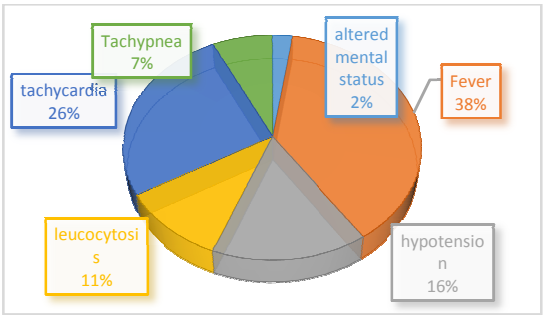

Figure 3: Shows the distribution of signs and symptoms of infection among the study patients

This table shows the various signs and symptoms of infection with which the patient presented at the time of admission. The commonest being fever and tachycardia

Table 6: Distribution of Infective source

	Frequency	Percentage
Nosocomial Infection		
abdominal distension	6	13.04
Abdominal pain	2	4.35
cardiac dysfunction	4	8.70
Cellulitis	1	2.17
congestive Cardiac failure	1	2.17
pyrexia of unknown origin	3	6.52
respiratory infection	6	13.04
IV line infection	2	4.35
Pregnancy related infection		
fetal demise	3	6.52
PPROM	3	6.52
PROM	1	2.17
peurperal sepsis	1	2.17
Episiotomy infection	4	8.70
Non-Pregnancy related infection		
Hepatitis	3	6.52
UTI	5	10.87
pyelonephritis	1	2.17
Total	**46**	**100.00**

This table represents the various sources of infections suspected in the patients with sepsis. The most common

being respiratory infections in nosocomial, episiotomy wound infection in pregnancy related and UTI in non-pregnancy related infections respectively.

Table 7: Distribution of Signs of Organ Dysfunction

	Frequency	Percentage
APTT>46.2	1	2
hyperbilirubinemia	4	8
INR>1.5	2	4
o2 for spo2<90%	4	8
thrombocytopenia	14	28
liver dysfunction	5	10
urea>44	1	2
urine output<0.5ml/kg/hr in 2hrs	1	2
None	18	36
Total	**50**	**100**

This table shows the various signs of organ dysfunction with which the patient presented with at the time of admission commonest sign being thrombocytopenia.

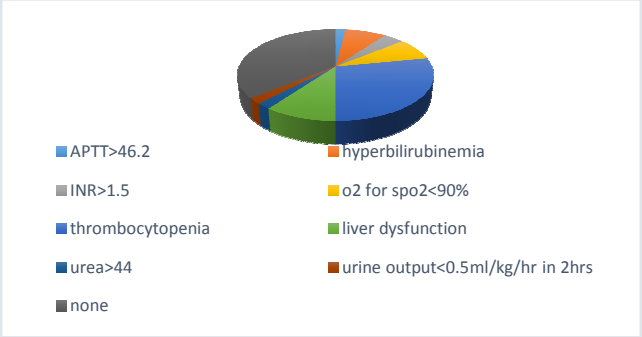

Figure 5: Shows the distribution of signs and symptoms of organ dysfunction among the study patients

Table 8: Distribution of Serum Lactate at admission

	Frequency	Percentage
Positive(≥2.2mmol)	14	35
Negative(<2.2mmol)	26	65
Total	**40**	**100**

This table represents the frequency and percentage of patients in whom lactate was positive or negative at the time of admission.

Table 9: Distribution of serum lactate in all patients at the time of admission

		Patients in Sepsis Other Criteria		
		Positive	**Negative**	**Total**
Serum Lactate at Admission	Positive	9	5	14
		64.29%	35.71%	100%
		40.91%	27.78%	35.00%
	Negative	13	13	26
		50.00%	50.00%	100%
		59.09%	72.22%	65.00%
	Total	**22**	**18**	**40**
		55.00%	**45.00%**	**100%**
		100%	**100%**	**100%**

This table represents the percentage and frequencies of admission lactate levels in patients with obstetric related sepsis.

Table 10: Efficacy of the serum lactate as a prognostic factor in sepsis

Sensitivity	Specificity	PPV	NPV	Agreement	Kappa	p value
53.8	100.0	100.0	53.8	70.0	0.450	0.001

This table proves that serum lactate is highly significant as a predictor of sepsis in obstetric related sepsis.

Table 11: Univariate analysis of serum lactate at admission

Table 12: Pairwise Comparisons of serum lactate

DISCUSSION

The present study was undertaken at Father Muller Medical College Hospital at mangalore from the years 2012-2014.The study was aimed at using serum lactate, a blood marker, as a prognostic factor of severe sepsis in both antenatal and postnatal patients who were admitted with sepsis.This study was conducted on 40 patients (both antenatal and postnatal) who had sepsis. In these patients sepsis was diagnosed if the patients met the inclusion criteria. Many studies have determined lactate as a significant prognostic factor in sepsis[3,4, 5] but its importance in obstetric related sepsis is yet ill defined. It is shown that the present study in which 40 patients were included, it was found that the common age group affected were those in the reproductive age between 20-35 years. These findings were similar to the studies conducted by Bardale [6] *et al*, Puri [7] *et al*, Prabha [8] *et al* and Shivakumar [10] *et al*. Whereas in a study conducted by Meharun [9] *et al* conducted in obstetric patients. It was found that a higher age group of >31 years were affected. The reason for a younger age group could be because this is the most common age group in our hospital. It shows that, in the present study, sepsis was more common. These findings were similar to studies conducted by Meharun *et al*. In other studies by Shivakumar[10] *et al* , Prabha *et al* [11]and Jaspinder *et al*[12] conducted in obstetric patients, primigravidas were more commonly affected. It shows that, no studies were found to determine the levels of serum lactate to diagnose severe sepsis in pregnancy, in the studies conducted by Krishna[4] *et al*, Green[3] *et al* and Londono[15] *et al.* in non obstetric patients, they used a serum lactate of ≥4mmol/L as the cut off to diagnose severe sepsis in patients admitted to the ED. Whereas Shapiro[7] *et al*, Stephen[5] *et al* and Mikkelsen[13] *et al.* in non obstetric patients, used lactate levels of ≥2-2.5mmol/L and this value was similar to that used in the present study which was ≥2.2mmol/L for the prediction of severe sepsis. It shows that, in the present study, initial lactate levels were sent for all patients in sepsis, those

with serially elevated lactate levels showed poor outcome requiring closer monitoring and prompt treatment, these findings were similar to a study conducted by Krishna[4] *et al*, where it was found that the probability of acute phase death and in-hospital death increased significantly and in a linear fashion with increasing range of serum lactate values over a period of time.Although there are many mechanisms of lactate generation, regardless of the cause, their study proved lactate was a marker of high risk of death which was true in the present study as well. It shows that, Krishna[4] *et al* and Londono[15] *et al* in their study established serum lactate as an independent and significant predictor of mortality in patients with severe sepsis but who were hemodynamically stable, these findings were contradictory to those of the present study because most of our patients were hemodynamically unstable, hence although serum lactate was used as a prognostic factor of severe sepsis along with other laboratory parameters, its significance as an independent predictor could not be effectively established. It shows that in a study conducted by Stephen[5] *et al*, with 1177 patients, where he used serum lactate as a predictor of mortality in patients with infection, the study showed a high specificity of 99% and a low sensitivity of 6%, this was similar in the present study which had a high specificity of 100% and low sensitivity of 53.8%. The reason for the low sensitivity could be due to the fact that many other variables played an important role in affecting the blood lactate levels in severe sepsis. In the present study serum lactate was used as the only determining factor of prediction in terms of severity of sepsis as in contrast to the study by Green[3] *et al* where lactate and CRP were used in the diagnosis of infection in patients admitted to the ED. In their study they proved that a combination of the above parameters had a higher prediction of mortality as compared to either one. Since CRP levels are usually elevated in obstetric related infections, its significance as a prognostic tool could not be determined. In a study by Brothwick[16] *et al*, isomers of lactate namely d or l-lactate were determined in ICU patients for predicting clinical outcomes, though no specific prognostic information could be derived, follow up of d-lactate levels rendered valuable results but needed further studies. In comparison our study did not use isomers of lactate hence no conclusion could be derived on the same. Krishna[4] *et al*, conducted a study which used serial lactate levels over a period of time as an early predictor of shock in patients of trauma or sepsis. In their study they repeated these serum lactate values at 12 and 24 hours respectively. They concluded that interventions to decrease elevated lactate values to normal, improved chances of survival in these patients. The present study also showed similar results as early detection and therapy lowered the serum lactate levels with simultaneous improvement of these patients as evident from the statistics on. Mikkelsen[13] *et al* in a study used varying ranges of venous lactate levels, such as low (<2), intermediate (2-3.9) or high (≥4), multivariable logistic regression analyses were stratified on the presence or absence of shock. They concluded that initial lactate level in intermediate and high levels were associated with mortality, independent of organ dysfunction and shock, this was similar to the findings in a study by Kang[18] *et al*. In the present study it was proved that high levels of lactate (>4) was invariably associated with multiorgan dysfunction and a higher risk of mortality and this was similar to Revelly[17] *et al*.

CONCLUSION

In the present study conducted at Father Muller Medical Hospital mangalore in the years August 2012 to July 2014 in 40 patients admitted to the hospital, it was found that admission serum lactate levels played an important role in the diagnosis of severe sepsis and can be used as an effective and independent predictor of sepsis.

REFERENCES

1. Centre for Maternal and Child Enquiries (CMACE). Saving Mother's Lives: reviewing maternal deaths to make motherhood safer: 2006-2008. *BJOG* 2011; 118(suppl. 1):1-203.
2. Dellinger RP, Levy MM, Rhodes A, Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock. Intensive Care Med 2013; 39(2): 165-228 and Crit Care Med 2013; 41(2): 580-637.
3. Green JP, Berger T, Garg N, Shapiro NI. Serum lactate is a better predictor of short-term mortality when stratified by C-reactive protein in adult emergency department patient's hospitals for a suspected infection. Ann Emerg Med. 2011 mar; 57(3):291-5.
4. Krishna U, Joshi SP, Modh M .An evaluation of serial blood lactate measurement as an early predictor of shock and its outcome in patients of trauma or sepsis. Indian J Crit Care Med. 2009 Apr-Jun; 13 (2); 66-73.
5. Stephen T, Dellinger RP, Michael EC, Ryan CA, Christa S, BM. Serum lactate as a predictor of mortality in patients with infection. Intensive care med 2007; 33:970-977
6. Bardale RV, Dixit PG, Pregnancy-related deaths: A three year retrospective study, J Indian Aca Forensic Medicine, 32(1)
7. Puri Alka , Yadav Indra, Jain Nisha, Maternal Mortality in an urban tertiary care hospital of north India. The Journal of Obsteterics and Gynaecology of India. May – June 2011 pg 280-285
8. Prabha S, Saswati N, Indranil S, Dilip KD, Deaths amongst women of reproductive age group in the gynaecology and obstetrics department of a tertiary care hospital of eastern India. Safety science monitor Vol 15, Issue 3.

9. Meharun NK, Shahla B, Aneela S, Risk factors and complications of puerperal sepsis at a tertiary healthcare centre. Pak J Med Sci. 2013 July – Aug; 29(4): 972-976
10. Shivakumar HC, Umashankar KM, Ramaraju HE, Shankar J, Analysis of maternal mortality in tertiary care hospital, International journal of basic and applied medical sciences 2013 Vol 3, May – Aug, pg; 237- 242
11. Prabha C, Jyoti L, Chauhan VK, Maternal mortality among tribal women as per gravidity at a tertiary level of care in Bastar Chhattisgarh,India. Int J Biol Med Res, 2012; 3(1): 1377-1384.
12. Jaspinder K, Kawaljit K, Obsteteric complications: Primiparity Vs Multiparity. European Journal of Experimental Biology, 2012, 2(5):1462 – 1468
13. Mikkelsen, Mark E, Miltiades, Andrea N, Gaieski, DF. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med. 2009; 37(5):1670-1677
14. Shapiro NI, Christopher F, Michael D, Lauren C, Aimee T, Stephen T. The feasibility and accuracy of point of care lactate measurement in emergency department patients with suspected. Infection J Emerg Med. 2010 July; 39(1);89-94
15. Londono J, Leon AL, Rodriguez F, Barrera L, Rosa G, Dennis R. Serum lactate in the emergency department as a prognostic factor in patients with sepsis without hypotension. Med Clin (Barc). 2012 Jul; 30
16. Borthwick HA, Brunt LK, Mitchem KL, Chaloner C. Does lactate measurement performed on admission predict clinical outcome on the intensive care unit? A concise systematic review. Ann Clin Biochem. 2012 jul;49(4):391-4
17. Revelly, Jean P, Tappy, Luc, Martinez, Alexandro, Bollmann, Marc, Cayeux, Marie RN, Berger MM, Chiolero, Rene L. Lactate and glucose metabolism in severe sepsis and cardiogenic shock. Critical care medicine, 2005 oct;33(10):2235-2240.

Source of Support: None Declared
Conflict of Interest: None Declared