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Measurement Of Umbilical Venous Lactate Levels For Predicting Poor Neonatal Outcomes

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Abstract

Objectives: To determine the utility of umbilical venous lactate measurements for predicting poor neonatal outcomes.
Method: This observational study was conducted at Kahuta Research Laboratories (KRL) hospital, Islamabad from May 2019 to October 2019. Singleton pregnancies with no known fetal congenital anomalies and gestational age greater than 28 weeks were included. Descriptive statistics were used to analyse the characteristics of study subjects and also composite neonatal outcomes. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated.
Result: Umbilical venous lactate levels were found to be highest in instrumental deliveries (48.7%) and lowest in those delivered by elective cesarean section (25.7%). Low APGAR score, need for initial resuscitation & neonatal intensive care unit admission, mechanical ventilation and neonatal morbidity were all associated with significantly higher lactate levels. Based on the maximal yield index, the optimal cut-off point for predicting neonatal morbidity was 46.5mg/dl (area under the receiver operating characteristics curve was 0.8). Based on this optimal cut-off point, it has a sensitivity of 62%, specificity of 92%, PPV 51% and NPV 94% for neonatal morbidity.
Conclusion: Umbilical venous lactate measurement is a good predictor of poor neonatal outcome especially in situations when umbilical arterial blood cannot be taken due to technical difficulty. Mode of delivery has a strong association with fetal hypoxia and raised umbilical lactate levels.

Keywords: lactate, neonatal outcomes, labour ward.

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1. Introduction

Perinatal asphyxia due to childbirth related events has long been associated with neonatal morbidity and mortality.[1] Studies have revealed that labour accounts for 7-15% of avoidable neonatal morbidity. The National Institute for Health and Clinical Excellence (NICE) states that vigilant monitoring during intrapartum period helps in early identification of babies at risk of perinatal asphyxia thus preventing long term neurological consequences.[2]

Lactate concentration occurs during hypoxic states as it is the end-product of anaerobic metabolism which contributes to the metabolic acidosis and irreversible fetal brain injury was first described by Myers et al. It is the fetus which contributes to the lactate concentration in the umbilical cord[3] thus making raised umbilical cord lactate levels as a marker of fetal hypoxia during labour. If perinatal asphyxia would be diagnosed early, timely rehabilitative measures might reduce the devastating long term outcomes.[4]

In recent years, lactate measurement in the umbilical cord blood has been shown to be a more sensitive predictor of fetal morbidity as compared to umbilical cord pH.[5] Studies have highlighted that umbilical cord lactate levels can be used as a marker for detection of Hypoxic Ischemic Encephalopathy (HIE).[6]

Several studies have been conducted in the developed world to define the reference ranges of umbilical arterial lactate levels but it is technically difficult to draw the arterial blood at the time of delivery due to small size of the artery (none of the comparative studies have been conducted so far).

Umbilical venous blood which can be more easily taken can be readily used to assess perinatal asphyxia but there are very limited studies conducted on it so far. Also due to the non-availability of local data, the current study was designed to determine the utility of umbilical venous lactate measurements for predicting poor neonatal outcomes in a labour ward of a tertiary care hospital.

2. Materials & Methods

After getting approval from the hospital's ethical committee, this observational study was conducted in collaboration with the Department of Obstetrics and

Gynaecology and the Department of Paediatrics, at Kahuta Research Laboratories (KRL) hospital, Islamabad over 6 months through a non-probability consecutive sampling technique between May 2019 to October 2019.

The sample size was calculated by the WHO Sample Size calculator (Sample Size Determination in Health Studies: a Practical Manual / S. K. Lwanga and S. Lemeshow) with the help of sensitivity = 87%, specificity = 91.3%, expected prevalence of poor neonatal outcome = 30.5%, precision level = 5%, confidence interval = 95%. The total sample size turned out to be 399.

A proforma was designed after an extensive literature review. Inclusion criteria included all the singleton pregnancies with no known fetal congenital anomalies, gestational age greater than 28 weeks and no known maternal medical comorbid. Exclusion criteria were multiple pregnancies, congenital fetal anomalies on anomaly scan, gestational age less than 28 weeks and maternal medical disorders. After taking verbal informed consent, participants were recruited for the study.

Gestational age was calculated according to the last menstrual period and it was confirmed by first and second-trimester ultrasound scans. Fetal heart rate trace using cardiotocography (CTG) was taken before the delivery of a baby and was classified as a reassuring, suspicious and pathological heart rate pattern according to the 2015 FIGO intrapartum cardiotocography (CTG) classification system. Duration of the second stage of labour was noted and the mode of delivery was grouped into vaginal delivery, instrumental delivery, elective and emergency cesarean section.

Umbilical venous blood was taken in a heparinised test tube, immediately after delivery of the baby and sent to the laboratory within 15 minutes as per manufacturer's recommendations of a radiometer analyser.

The composite neonatal outcomes included APGAR score at 1 and 5 minutes, the need for resuscitation, neonatal intensive care unit admissions and any neonatal morbidity during the first 7 days of life (meconium aspiration syndrome, respiratory distress syndrome, hypoxic-ischemic encephalopathy and early neonatal death). The neonatal outcomes were diagnosed by the attending paediatrician. The neonatal morbidity was used as a criterion of whether or not the newborn suffered from perinatal asphyxia.

Descriptive statistics were used to analyse the characteristics of study participants and also composite neonatal outcomes. The optimal cut-off point of lactate for predicting neonatal morbidity (neonatal morbidity is explained in results in the form of hypoxic-ischemic encephalopathy, meconium aspiration syndrome, respiratory distress syndrome and mechanical ventilation need) was taken based on maximal youden index[7] and receiver operating characteristic (ROC) curve was used to determine the area under the curve. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated at the optimal cut-off point of lactate by comparing it with neonatal morbidity.

Results were analysed using the Statistical Package for Social Sciences (SPSS) version 19. P value less than 0.05 was considered statistically significant.

3. Results

A total of 399 singleton pregnancies fulfilling the inclusion criteria were analysed during the study period. Descriptive data on the study participants is shown in Table 1.

Table 1: Descriptive data on study participants (n=399)

Variables		No of participants (n)	Percentage (%)
Gestational age (weeks)	>37	344	86.2
	32-32+6	50	12.5
	28-31+6	5	1.3
Cardiotocography (CTG)	Reassuring	351	88
	Suspicious	27	6.8
	Pathological	21	5.3
Duration of the second stage of labour (minutes)	<30	94	23.6
	30-60	39	9.8
	60-90	2	0.5
	>90	0	
Mode of delivery	SVD	122	30.6
	Forceps	7	1.8
	Vacuum	5	1.3
	Em.LSCS	91	22.8
	El.LSCS	174	43.6

The majority of the participants were at term gestation. Suspicious and pathological CTG was present in 12.1% of participants. During labour, many participants ended up in Emergency LSCS before full dilatation of the cervix (22.5%). The predominant mode of delivery was Elective LSCS.

Umbilical lactate levels were found to be highest in instrumental deliveries (forceps and vacuum) and lowest in those delivered by Elective LSCS. Mean umbilical

lactate levels in the instrumental deliveries were 48.7mg/dl ± SD19 and 47.6mg/dl ± SD17.5 (forceps and vacuum). Spontaneous vaginal delivery (SVD) had the second highest mean umbilical lactate values (36.5mg/dl ± SD 17.4) followed by Emergency LSCS (32.8mg/dl ± SD 16.0) and Elective LSCS (25.7mg/dl ± SD 10.7).

Similarly, umbilical venous lactate concentration was increased with increasing the duration of the second stage of labour. Mean umbilical lactate levels were 32.8mg/dl ± SD 7.0 in those who had a second stage of labour less than 30 minutes versus 48.1mg/dl ± SD 12.1 whose second stage lasted for more than 30 minutes.

Reassuring CTG trace was associated with lower umbilical lactate levels whereas high lactate levels were found in those who had pathological CTG trace immediately before delivery, as shown in Table 2

Table 2: Distribution of mean Umbilical cord lactate levels according to the mode of delivery

Variables	Mean umbilical cord lactate levels (in mg/dl) ± SD
Forceps delivery	48.7 ± 19
Vacuum delivery	47.6 ± 17.5
Spontaneous vaginal delivery	36.5 ± 17.4
Emergency LSCS	32.8 ± 16.0
Elective LSCS	25.7 ± 10.7

The distribution of the components of the composite neonatal outcomes is tabulated in Table 3. There were 77 admissions in the neonatal intensive care unit during the study period and the main reasons were low APGAR scores and the need for mechanical ventilation. Low APGAR score, the need for initial resuscitation & NICU admission, mechanical ventilation and neonatal morbidity were all associated with significantly higher mean venous lactate levels. ROC (Receiver Operating Curve) is a graphical representation of the diagnostic ability of binary classifiers.

In our study, the ROC curve is representing the diagnostic ability of venous lactate levels as a trade-off between sensitivity and specificity.

The closer the curve to the 45-degree diagonal of ROC space, the less accurate the test. As our curve is more towards the left side, which means it has more accuracy. Based on the maximal Youden index, the optimal cut-off point for predicting neonatal morbidity was 46.5mg/dl (area under the ROC curve 0.8) as shown in Figure 1.

Table 3: Distribution of the components of composite neonatal outcomes (n=399)

Components		No of participants (n)	Percentage (%)
Apgar scored at 1minute	>7	324	81.2
	4-7	72	18
	<4	3	0.8
Apgar scored at 5minutes	>7	389	97.5
	4-7	10	2.5
	<4	0	
Resuscitation	Yes	23	5.8
	No	376	94.2
NICU admissions	Yes	77	19.3
	No	322	80.7
Neonatal morbidity in the first 7 days of life	HIE	8	2
	MAS	1	0.3
	RDS	12	3
	Mechanical ventilation	26	6.5
Status at discharge from hospital	Alive	396	99.2
	Expired	3	0.8

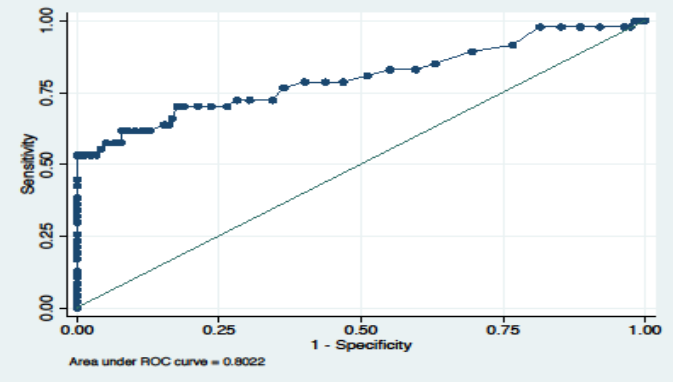

Figure 1: Reciever operating characteristics (ROC) curve

Based on this optimal cut-off point, it has a sensitivity of 62%, specificity of 92%, PPV of 51% and NPV of 94%.

4. Discussion

This study has highlighted that raised umbilical lactate levels have a positive correlation with pathological cardiotocography, prolonged duration of the second stage of labour, instrumental deliveries and poor neonatal outcomes. The optimal cut-off point of 46.5mg/dl for umbilical venous lactate has a good specificity and NPV.

Advancing gestational age has no association with raised umbilical lactate levels which is in contrast to the results of a study by Wiberg N et al which found high lactate levels in cord blood of babies born at term due to their high glycolytic activity as compared to preterm babies.[8]

According to Nordstrom L, high glycolytic activity in the presence of aerobic conditions does not affect umbilical lactate concentrations.[9]

Pathological cardiotocography is an indication of immediate delivery as it reflects perinatal asphyxia. In the presence of anaerobic conditions, lactate production is increased to meet energy requirements. This study showed high mean umbilical lactate values in babies who had suspicious or pathological cardiotocography which is in line with the results of a study by Hamed HO which highlighted the significant association between late and prolonged decelerations and raised lactate levels.[10]

Vaginal delivery induces the release of catecholamines due to stress of labour. The more prolonged the labour is, the more catecholamines are produced especially during the second stage of labour. To meet the energy requirements, there is enhanced fetal glycogenolysis and a shift to anaerobic metabolism resulting in lactic acidaemia.[11] Our study strengthened the results of a study by Mokarami P et al that umbilical lactate levels increase with increasing duration of the second stage of labour.[12]

Amongst vaginal deliveries, our study showed that instrumental vaginal deliveries were associated with significantly higher mean lactate values than spontaneous vaginal deliveries which paralleled the results of a study by Subramaniam RN.[13] This is because the commonest indication for instrumental deliveries is fetal distress which causes perinatal asphyxia by inducing lactic academia. Lowest cord blood lactate levels were found in babies delivered by elective cesarean section as they are protected from labour-related stress and anaerobic metabolism associated with lactic acidaemia. Similar results were found in other studies.[13]

The neonatal outcomes are usually measured in terms of APGAR score at 1 and 5 minutes. A low APGAR score at 1 minute reflects short-term morbidity and a low APGAR score at 5 minutes is reflective of long-term morbidity. We found in our study that those babies who suffered from perinatal asphyxia had low Apgar scores at 1 and 5 minutes and high umbilical lactate levels. The majority of these babies needed initial resuscitation, and neonatal intensive care unit admissions and developed neonatal morbidity in terms of HIE, RDS or MAS. A study conducted by Martin A demonstrated no significant association between high umbilical lactate levels and immediate neonatal morbidity[14] which is in contrast to the results of our study but several new studies have revealed a positive correlation between high umbilical lactate levels and neonatal morbidity.[15,16]

Some studies have highlighted that high lactate levels have an association with male gender and primigravidity, but our study has not included these demographic details.[17] Various studies have highlighted the optimal cut-off point of umbilical cord lactate which should be used as a predictor of neonatal morbidity. Our study found a cut-off value of 46.5mg/dl for umbilical venous lactate with a sensitivity of 62%, specificity of 92%, PPV of 51% and NPV of 94% for neonatal morbidity. Similar studies have demonstrated varying cut-off points for neonatal morbidity ranging from 27mg/dl[15] to 97.2mg/dl[16] for arterial or venous umbilical lactate levels. The optimal cut-off point of umbilical venous lactate level taken in our study showed that it is not sensitive enough to pick up all the cases of perinatal asphyxia but it is highly specific that if the value is above this cut-off point, the baby will suffer from neonatal morbidity. PPV of 51% and NPV of 94% highlight that the babies with high umbilical lactate levels will not necessarily develop neonatal morbidity but if the lactate levels are below this cut-off point, then the likelihood of neonatal morbidity will be extremely low. A good specificity and high NPV make it an ideal test in cases of deliveries complicated by fetal distress so that early detection and treatment of those babies can prevent them from respiratory and long-term neurological morbidity.

5. Conclusion

Pathological cardiotocography, duration of the second stage of labour and mode of delivery have strong associations with fetal hypoxia and raised umbilical lactate levels. Keeping in mind the low cost of the test and easy sampling technique, it should be employed in labour wards of resource-limited countries like Pakistan.

CONFLICTS OF INTEREST- None

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Contributions:

M.H, M.A.Q, I.S - Conception of study
M.H, M.A.Q, I.S - Experimentation/Study Conduction
M.H, M.A.Q - Analysis/Interpretation/Discussion
M.H, M.A.Q - Manuscript Writing
I.S - Critical Review
I.S - Facilitation and Material analysis

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

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