

APGAR score and umbilical cord blood levels of Lactate and Creatinine in Perinatal asphyxia

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Abstract

Objective: APGAR score and umbilical cord blood levels of Lactate and Creatinine in Perinatal asphyxia.

Design: Descriptive cross sectional study.

Setting: Labour room of Medical College Hospital, Thrissur, Kerala.

Subjects: 128 babies born during two months period (April – May 2008) were included in the study.

Outcome measures: Well being of the new born assessed by the clinical criterion, Apgar score and severity of asphyxia in the new born assessed by cord blood lactate and creatinine.

Results: Reference limits and clinical decision limits of lactate (12- 76 mg%; 27mg %) and creatinine (0.60-1.4 mg%; 0.81 mg %) were found out. The clinical decision limit of lactate obtained in the study (27 mg %) was found to be significantly associated with perinatal asphyxia diagnosed by Apgar score. Sensitivity and specificity of cord blood lactate at the cut off value of 27 mg% is 68% and 60 % respectively (AUC = 0.679 P = 0.0001)

Whereas for creatinine the clinical decision limit obtained was 0.81 and at this level +ve LR and -ve LR were 1.34 and 0.59 respectively. The area under ROC curve (AUC) was 0.576 but it did not achieve statistical significance (P = 0.1336)

Conclusion: Cord blood lactate assay of new born will help to evaluate the severity of anoxia and it will be useful to nullify any subjective errors produced during the clinical assessment of newborn babies by Apgar score.

Keywords: Perinatal asphyxia, Apgar score, Cord blood lactate and creatinine

1. Introduction

Perinatal period extends from 22 completed weeks of gestation to less than 7 days of life, after birth. Perinatal asphyxia exists when an ante partum event, labor or birth process diminishes the oxygen supply to the fetus, causing decreased fetal or newborn heart rate, which results in the impairment of exchange of respiratory gases oxygen(O₂) and carbon dioxide(CO₂) and inadequate perfusion of tissues of major organs. The outcome of perinatal asphyxia includes immediate complications like hypoxic ischemic encephalopathy, shock or even death and long term problems like mild cognitive defects, seizure disorders and mild to severe neurological disability.

It is difficult to accurately assess the incidence of perinatal asphyxia because of non uniform clinical criteria on which different institutions base their definition. The incidence of asphyxia varies between 1% and 5% depending on the criteria used in making the diagnosis.[1] There is no ideal measure to assess perinatal asphyxia in clinical practice. The commonly used Apgar score has been shown to be not specific for hypoxia and has a weak relationship with biochemical evidence of asphyxia.[2][3][4]

A low Apgar score may also be related to factors other than perinatal asphyxia like gestational

age, maternal medication and anesthetic administration. A low Apgar score might identify newborns that need resuscitation but cannot be correlated with long term outcome. The study of Borruto *et al*[5] showed that evidence of clinical fetal distress is not related to severity of hypoxia.

The challenge is to identify markers that can help to nullify the subjective errors that may arise while using APGAR score to diagnose asphyxia in new born clinically and to predict the risk of future problems objectively. Lactate in the cord blood, the specific end product of anaerobic metabolism may have the potential for this purpose. It is wiser to rely on two efficient parameters than a single one to make a critical diagnosis of a disease. Cord blood Creatinine may serve this purpose. Perinatal asphyxia leads to under perfusion of the kidneys resulting in reduced glomerular filtration rate which in turn causes elevation of creatinine in the body fluids.[6]

We sought to evaluate whether increasing levels of cord blood lactate and cord blood creatinine are associated with perinatal asphyxia by using the commonly practised APGAR score as the gold standard and if so to validate the diagnostic efficacy of cord blood lactate and cord blood creatinine levels over Apgar score in perinatal asphyxia.

2. Methods

We performed a descriptive cross sectional study at Medical College Hospital, Thrissur. 128 babies born over a period of two months were included in the study. A proforma was prepared to collect relevant information of each baby. Approval was obtained from institutional ethics committee. Informed written consent was obtained from the parents of the babies considered for the study.

Apgar score was used to differentiate normal babies and those babies subjected to asphyxial insult.

2.1 Measurements

Clinical assessment of well being of the baby done by APGAR score at 1 minute. Biochemical parameters umbilical cord blood lactate[7]and creatinine[8] were assayed by colorimetric technique in a semiautomatic analyzer.

2.2 Specimen: Cord blood

2.3 Data analysis

Apgar score was used to identify perinatal asphyxia in the new born. Those babies with apgar

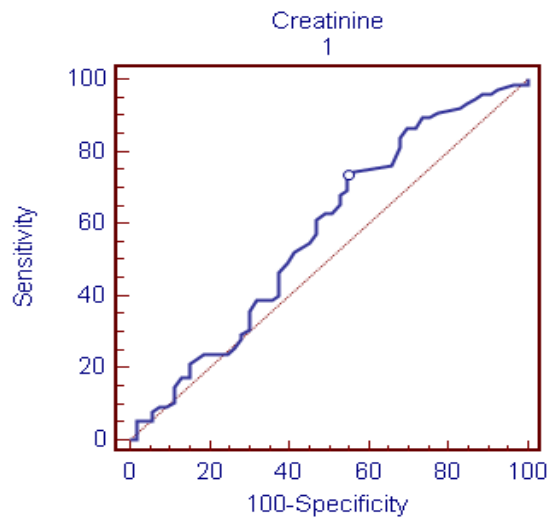
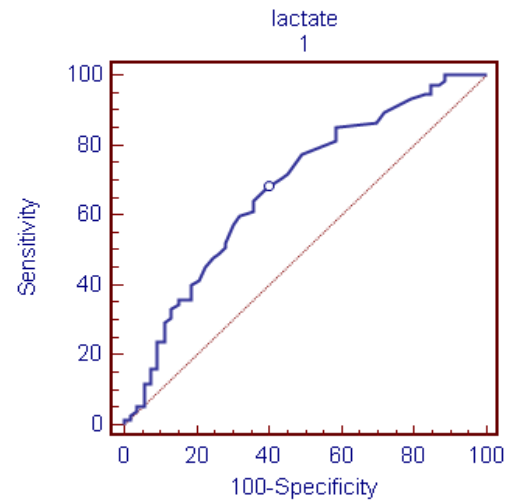
score of ≤ 7 were considered to have had perinatal asphyxial insult and those with ≥ 8 were taken as normal. The latter were the reference babies for validating the biochemical parameters against the gold standard apgar score in diagnosing perinatal asphyxia. The guide line (non parametric method) recommended by the National committee for Clinical Laboratory Standards(NCCLS)[9] was used to determine the reference intervals of lactate and creatinine in the cord blood. Receiver-operating characteristic curve (Med CALC) was employed to know the clinical decision limit and diagnostic ability of these biochemical variables to diagnose perinatal asphyxia. The cut off values thus obtained for lactate and creatinine were used in the further validation of these biochemical variables (sensitivity, specificity, likelihood ratios and predictive values) by comparison with Apgar score taken as the gold standard.

3. Results and Discussion

During the two months study period 128 new born babies were evaluated for perinatal asphyxia in terms of I minute Apgar score, cord blood lactate and creatinine. Those babies with Apgar score ≥ 8 were considered not subjected to anoxic insult and those with the score ≤ 7 were considered to be subjected to asphyxia.

Apgar score was used as the criterion to find out the newborn not subjected to asphyxial insult (reference group; n=115).The values of lactate and creatinine obtained from this reference group were considered as reference values for the determination of reference interval. For the 115 reference values, the rank of the 2.5th percentile observation (as per NCCLS Guideline document) was 2.9 ($0.025 \times 116 = 2.9$) and the rank for 97.5th percentile observation was 113($0.975 \times 116 = 113$); these are indicated in the table 1 as * and ** respectively. These rank values were used to estimate upper and lower reference limits and the 95% reference interval obtained was 12 -76mg% for cord blood lactate and 0.6 – 1.4 mg% for cord blood creatinine.

Optimal cut off value or medical decision limit for these laboratory parameters were selected by receiver- operating characteristic (ROC) curves. (see Figure 1 and 2) .It was 27 mg % for cord blood lactate with a sensitivity 68%, specificity 63.38%, +ve LR (likelihood ratio) 1.72, -ve LR 0.53, positive predictive value (PPV) 70.8 and negative predictive value (NPV) 57.1(see Table 3).

Figure 1: ROC (Receiver –operating characteristic) curves of cord blood Creatinine in the diagnosis of Perinatal asphyxia**Figure 2: ROC (Receiver –operating characteristic) curves of cord blood Lactate in the diagnosis Perinatal asphyxia****Table 1: Frequency distribution of 115 neonates with Apgar score ≥ 8**

Lactate mg%	Frequency	Lactate mg%	Frequency	Creatinine mg%	Frequency
7.6	1	36	2	0.3	1
11	1	37	3	0.4	1
12*	4	38	3	0.6*	9
13	1	40	2	0.7	10
15	2	41	2	0.8	30
16	1	42	2	0.9	25
17	2	43	1	1	18
18	1	44	1	1.1	10
19	3	45	2	1.2	6
20	7	46	2	1.3	2
21	3	49	2	1.4**	3
22	7	50	2	-	-
23	3	52	1	-	-
24	8	53	2	-	-
25	6	54	2	-	-
26	2	55	1	-	-
27	4	57	1	-	-
28	5	58	1	-	-
30	2	59	1	-	-
31	3	60	1	-	-
32	2	66	1	-	-
33	5	72	1	-	-
34	1	76**	1	-	-
35	2	86	2	-	-

As per National Committee for Clinical Laboratory standards¹⁸*Indicates 2.5th percentile **Indicates 97.5th percentile

Table 2: Efficacy of cord blood creatinine in the diagnosis of perinatal asphyxia

Area under the ROC curve (AUC)	0.576
95% Confidence interval	0.486 to 0.663
Significance level P (Area=0.5)	0.1336
Sensitivity	73.33
Specificity	45.28
+ *LR	1.34
- *LR	0.59

If the cord blood lactate value is more than 27 mg%, there is a 70.8 % (PPV 70.8) chance of suffering from anoxia but if it is less than 27 mg% , there is 57.1 % (N PV 57.1) probability of not having been subjected to asphyxia. Low PPV is acceptable in this clinical context (70.8) because treatment of a baby with false positive result will not produce any adverse consequences. Perinatal asphyxia is a serious condition which should not be missed since it may cause immediate multi organ

involvement or late neurological sequelae. Over diagnosis by false positive test will not create any psychological or economic trauma to the family.

For cord blood creatinine the clinical decision limit obtained was 0.81 mg% with sensitivity of 73.33% and the specificity 45.28 %. (See Table-2) but it did not achieve the statistical significance. This may be due to underrepresentation of relevant cases in the study.

Early recognition and prompt treatment often save the baby from developing neurological sequelae. In this context cord blood parameters are better than urinary parameters. Oliguria and increased β_2 microglobulin are also associated with cerebral abnormalities with perinatal asphyxia[6], but a period of 36 hours is required to record the degree of oliguria, a delay that hinders early diagnosis.

4. Conclusion

Reference interval of cord blood lactate is found to be 12- 76 mg% (95% confidence interval) and the clinical decision limit obtained is 27 mg%. Umbilical cord blood lactate will give an idea about the impact of anoxia in tissues. Being an objective parameter, it will be more convenient for confirming the diagnosis of asphyxia and for further follow up. It can be used to supplement APGAR score routinely.

Cord blood creatinine did not achieve statistical significance to diagnose perinatal asphyxia in the present study.

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