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ORIGINAL ARTICLE

Diagnostic Accuracy of Serum Creatine Kinase Muscle Brain Fraction and Lactate Dehydrogenase for Detection of Perinatal Asphyxia in Term Neonates

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ABSTRACT

Objective: To assess the diagnostic accuracy of serum creatine kinase muscle brain fraction and lactate dehydrogenase for detection of perinatal asphyxia in term neonates using clinical findings as Gold standard

Design of the Study: Cross sectional study

Study Settings: The study was conducted at Pediatric Department, Lahore General Hospital, Lahore from June 2021 to December 2021.

Material and Methods: Demographic information (name, age (in hours), gender, birth weight, and gestational age) was gathered. Under aseptic conditions, blood was taken with a 3cc BD syringe. For CK-MB and LDH testing, samples were sent to the pathology laboratory at the hospital. Two millilitres of clotted blood were tested using reagent kits and auto analyzers. Patients were classified as either positive or negative (according to the operational definition) based on the results of the evaluations of their reports.

Results of the Study: In our study, age distribution shows that 63.33%(n=152) were upto 6 hours and 36.67%(n=88) had >6 hours, mean+sd was calculated as 5.60+1.79 hours, 39.17%(n=94) were male and 60.83%(n=146) were females. The diagnostic accuracy of Serum Creatine kinase muscle brain fraction for detection of perinatal asphyxia in term neonates using clinical findings as gold standard was recorded as 93.59% sensitivity, 66.67% specificity, 99.10% positive predictive value, 21.05% negative predictive value and 92.92% accuracy rate.

Conclusion: For detecting prenatal asphyxia in term infants, the diagnostic accuracy of serum creatine kinase muscle brain fraction and lactate dehydrogenase (LDH) is useful, however LDH is more accurate than serum creatine kinase muscle brain fraction

Keywords: Perinatal asphyxia, detection, diagnostic accuracy

INTRODUCTION

A foetus or baby suffering from perinatal asphyxia, a condition in which crucial organs are deprived of oxygen or blood flow, has suffered an injury. the failure of a newborn to commence and maintain breathing, is referred to as birth asphyxia by the World Health Organization.[1] Neonatal HIE mortality and morbidity rates in underdeveloped nations are 100-250/1000 live births, compared to 5-10/1000 live births in the developed world, making it the major cause of death and disease among newborns.[2] Pakistan accounts for 7% of global neonatal deaths and birth asphyxia, found in 23% of neonates.[3] These Statistics reflect the magnitude of problem in Pakistan.

The diagnosis of perinatal asphyxia is routinely based on history of delayed or no cry at birth and poor Apgar scores. Biochemical markers that can determine the HIE & its stage before clinical manifestations appear, will be of great help.[5] Skyes et al in a study of 1110 newborns stated that APGAR score does not usually reflect the degree of acidosis at delivery, its value in asphyxia assessment must be questioned.[4]

Biochemical markers of asphyxia such as CK-MB and LDH have been studied in neonates who have had prenatal asphyxia, which can cause temporary myocardial ischemia and myocardial dysfunction.[6,7] The sensitivity and specificity is reported in a study of CK-MB were 28% and 100% while of LDH were 59.18% and 92% for prediction of perinatal asphyxia. This showed high specificity but very low sensitivity in neonate with Apgar score <7 and required resuscitation.[5] Another study also showed that the CK-MB has 30% sensitivity with a specificity of 100% while LDH has 96.3% sensitivity with a specificity of 87.9%.[8] The gold standard used in this study with be the APGAR score and clinical findings.

Rationale of this study is to assess the diagnostic accuracy of serum CK-MB and LDH for prediction of perinatal asphyxia in term neonates. In newborn, to rectify chances of perinatal asphyxia, an early and less invasive method is required to predict perinatal asphyxia. Literature showed that LDH is more accurate than CK-MB in predicting perinatal asphyxia. But controversial results have been noticed while there is a lack of local evidence. So implication of these markers in local set-up is not under working. So, through this study we want to establish a practice of conducting CK-MB and LDH for prediction of perinatal asphyxia on early basis. Moreover, which method is more reliable is also a debate. So we want to conduct this study to get local evidence and apply more reliable method in local set-up in future

MATERIAL AND METHODS

After receiving approval from the hospital's ethical committee the study was carried out. Patients reporting to the Pediatric Department, Lahore General Hospital, Lahore from June 2021 to December 2021

It is estimated that there will be 240 cases of prenatal asphyxia with a 95 percent confidence level and 23 percent predicted percentage of perinatal asphyxia, with the sensitivity of LDH being 59.18% with 13 % margin of error and the specificity being 92%.[5] Term neonates of either gender suspected with delayed cry at birth (cutt off 2 minute) or poor neonatal reflexes were suspected to have-asphyxia were included in this study. Neonates with very low birth weight neonate (<2000 grams), congenital malformation (on clinical examination), history of maternal drug addiction, coagulation disorders (PT>15sec, aPTT>20sec), septicemia (on blood culture) were excluded from the study.

A total of 240 newborns who met the inclusion criteria were enrolled in the study at Lahore General Hospital's emergency paediatrics department. Parents gave their permission for the procedure to proceed. Demographic information (name, age (in hours), gender, birth weight, and gestational age) was gathered. Under aseptic conditions, blood was taken with a 3cc BD syringe. The pathology lab at the hospital tested the samples for CK-MB and LDH. Samples were analyzed by reagent kits & auto analyzers

on 2ml of clotted blood. Reports were assessed and patients were labeled as positive or negative for both markers. Then neonates were admitted in NICU. If perinatal asphyxia develops then neonate was confirmed as positive or negative. All information was recorded on proforma.

The data was analysed with SPSS version 21 and all findings were documented in standard proforma. There was a mean and a standard deviation (SD) for quantitative variables like gestational age, birth weight, gestational age. Perinatal asphyxia (CK-MB, LDH, and real development) by frequency and percentage. Qualitative variables The sensitivity, specificity, PPV, NPV, and diagnostic accuracy of CK-MB and LDH were determined using 2x2 tables. Age, gender, gestational age, and birth weight of the neonate were taken into account when analysing the data. CK-MB and LDH sensitivity, specificity, PPV, NPV, and diagnostic accuracy were calculated using 2x2 tables generated after stratification.

STUDY RESULTS

Age distribution shows that 63.33%(n=152) were upto 6 hours and 36.67%(n=88) had >6 hours, mean±sd was calculated as 5.60+1.79 hours. Gender distribution shows that 39.17%(n=94) were male and 60.83%(n=146) were females. Mean birth weight (kgs) 2.74±0.46 kgs. Gestational age was calculated as 79.17%(n=190) were between 37-38 weeks had 20.83%(n=50) had >38 weeks as shown in table 1.

Frequency of perinatal asphyxia on gold standard was recorded in 97.5%(n=234) whereas 2.5%(n=6) had no findings of perinatal asphyxia. Frequency of perinatal asphyxia on CK-MB was recorded in 92.08%(n=221) whereas 7.92%(n=19) had no findings of perinatal asphyxia. Frequency of perinatal asphyxia on LDH was recorded in 77.92%(n=187) whereas 22.08%(n=53) had no findings of perinatal asphyxia. Diagnostic accuracy of Serum Creatine kinase muscle brain fraction for detection of perinatal asphyxia in term neonates using clinical findings as gold standard was recorded as 93.59% sensitivity, 66.67% specificity, 99.10% positive predictive value, 21.05% negative predictive value and 92.92% accuracy rate, using 2x2 Table shown in table 2 & 3.

Testing LDH's perinatal asphyxia detection precision in term neonates was found to be 98.40 percent sensitive, 92.31% specific, 79.00% positive predictive value, 57.14% negative and 78.05% accurate utilising gold standard clinical findings. The ninth table in the series Age, gender, gestational age, and birth weight of the neonate were taken into account when analysing the data. CK-MB and LDH sensitivity, specificity, PPV, NPV, and diagnostic accuracy were calculated using 2x2 tables generated after stratification as shown in table 4.

Table 1: Demographics of the study cases

Parameter	Sub-division	Frequency	Percentage
Age	Years	Mean±SD	5.60+1.79
	Upto 6	152	63.33
	> 6	88	36.67
Gestational age (weeks)	37-38	190	79.17
	>38	50	20.83
Birth weight	Kgs	Mean±SD	2.74±0.6
Gender	Male	94	39.17
	Female	146	60.83

Table 2: Frequency of Perinatal Asphyxia on Gold Standard, CK-MB & LDH

Parameter	Details	Frequency	Percentage
Perinatal asphyxia on Gold Standard	Yes	234	97.5
	No	6	2.5
Perinatal asphyxia On CK-MB	Yes	221	92.08
	No	19	7.92
Perinatal asphyxia On LDH	Yes	187	77.92
	No	53	22.08

Table 3: Sensitivity, specificity and predictive values of CK-MB and LDH

Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy
CK-MB	93.59%	66.67%	99.10%	21.05%	92.92%
LDH	98.40%	92.31%	79.40%	57.14%	78.75%

Table 4: Stratification of Creatinine Kinase Muscle Brain function (CK-MB) and Lactate Dehydrogenase (LDH) with different variables

Variables	Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
Serum Creatinin Kinase Muscle Brain Function							
Age	Upto 6 h	100%	50%	98.67%	100%	98.68%	0.000
	> 6 h	82.56%	100%	100%	11.76%	82.95%	0.003
Gender	Male	83.33%	50%	97.40%	11.76%	81.91%	0.09
	Female	100%	100%	100%	100%	98.63%	0.00
Gestational Age	37-38 weeks	91.85%	66.67%	98.83%	21.05%	91.05%	0.00
	>38 weeks	100%	00	100%	00	100%	0.00
Birth Weight	upto 2.5 kg	100%	0%	97.62%	0%	97.62%	0.00
	>2.5 kg	90.13%	100%	100%	21.05%	90.38%	0.00
Lactate Dehydrogenase (LDH)							
Age	Upto 6 h	100%	100%	100%	100%	100%	0.00
	> 6 h	92.50%	00	43.53%	00	42.05%	0.05
Gender	Male	97.40%	11.76%	83.33%	50%	81.91%	0.09
	Female	99.10%	5.71%	76.92%	66.67%	76.71%	0.08
Gestational Age	37-38 weeks	97.83%	7.69%	73.77%	57.14%	73.16%	0.07
	>38 weeks	100%	00%	100%	00%	100%	-
Birth Weight	upto 2.5 kg	100%	100%	100%	100%	95.70%	0.00
	>2.5 kg	97.17%	4.00%	68.21%	40%	67.31%	0.69

DISCUSSION

Literature showed that LDH is more accurate than CK-MB is predicting perinatal asphyxia. But controversial results have been noticed while there is a lack of local evidence. So implication of these markers in local set-up is not under working.[9,10,11,12,13] So, through this study we wanted to establish a practice of conducting CS-MB and LDH for prediction of perinatal asphyxia on early basis. Moreover, which method is more reliable is also a debate. So this study was to get local evidence and apply more reliable method in local set-up in future.

In our study, age distribution shows that 63.33%(n=152) were up to 6 hours and 36.67%(n=88) had >6 hours, mean±sd was calculated as 5.60+1.79 hours, 39.17% (n=94) were male and 60.83%(n=146) were females. The diagnostic accuracy of Serum Creatine kinase muscle brain fraction for detection of perinatal asphyxia in term neonates using clinical findings as gold standard was recorded as 93.59% sensitivity, 66.67% specificity, 99.10% positive predictive value, 21.05% negative predictive value and 92.92% accuracy rate. Diagnostic accuracy of LDH for detection of perinatal asphyxia in term neonates using clinical findings as gold standard was recorded as 98.40% sensitivity, 92.31% specificity, 79.40% positive predictive value, 57.14% negative predictive value and 78.75% accuracy rate.

Previous studies reported that the sensitivity and specificity of CK-MB were 28% and 100% while of LDH were 59.18% and 92% for prediction of perinatal asphyxia. This showed high specificity but very low sensitivity in neonate with Apgar score <7 and required resuscitation.[5] Another study also showed that the CK-MB has 30% sensitivity with a specificity of 100% while LDH has 96.3% sensitivity with a specificity of 87.9%.[8] Our findings are close to this study.

Another study[14] evaluated the diagnostic utility of a set of laboratory tests in the retrospective diagnosis of birth asphyxia and to study the association of laboratory markers of cardiac injury with the severity of perinatal asphyxia andat 8 hours, the cut-off CK-MB value of >92.6 U/L had 82% sensitivity and 82% specificity. In terms of positive and negative predictive values, CK-MB comes in at 80.34 percent and 81.63 percent, respectively. >60 U/L of CK-MB at 24 hours has a 58.33 per cent sensitivity and a 95.83 per cent spcificity cut-off value. There is a positive predictive value of 93.33 percent and a negative predictive value of 69.70 percent with the use of C-KMB. At 72 hours, a cutoff LDH value of >580 U/L has 100% sensitivity and 88% specificity. There are 89.29% of cases where LDH will be helpful, while the odds of it being harmful are 100%. Analysis of CKMB and LDH levels at 8 and 24 hours of life can differentiate between an asphyxiated and non-asphyxiated baby, based on the history and clinical aspects of the neonate, according to the researchers. The diagnostic performance of LDH is better than CK-MB. Results of our study are also comparable with the findings of Shylaja et al. (2014)[14], Jahan et al. (2019)[15], Meena et al. (2017)[16] and Doandes et al. (2017)[17].

CONCLUSION

For detecting prenatal asphyxia in term infants, the diagnostic accuracy of serum creatine kinase muscle brain fraction and lactate dehydrogenase (LDH) is useful, however LDH is more accurate than serum creatine kinase muscle brain fraction..

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