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Association of cord blood total creatine kinase activity with mode of delivery and APGAR score

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Abstract

Background: Creatine kinase (CK), an enzyme with an important role in consumption and saving energy, especially in muscle tissue. Increased CK is predominantly used to diagnose acute myocardial infarction, Neuromuscular disorders including myopathies, muscular dystrophy, rhabdomyolysis, drug-induced myopathies etc. During child birth, several fold changes in maternal total serum CK activity is observed. **Objective:** Our study aimed to correlate total CK activity with mode of delivery and APGAR score in newborns. **Methods:** This was an eighteen months hospital based descriptive study conducted by using a structured data collecting tool. The data were analyzed using SPSS software. **Results:** Out of 100 newborns, 51 were delivered by full term normal vaginal delivery (FTND) and 49 by lower segment cesarean section (LSCS). Maximum mothers were in the age group of 21 to 30 years. Birth weight of most of the newborns ranged between 2.5-3.0 kgs. We observed elevated total CK activity in both the modes of delivery. Significantly higher total CK activity ($p<0.001$) was observed in LSCS cases as compared to FTND cases. With decreasing APGAR score, a significant increase ($p<0.001$) in total CK activity was observed at both 1min and 5 min. **Conclusion:** Our study revealed that LSCS mode of delivery and lower APGAR scores are associated with increased CK activity..

Keywords: CK, APGAR score, LSCS, FTND.

INTRODUCTION

Optimal Creatine kinase (CK) is an enzyme with an important role in consumption and saving energy, especially in muscle tissue. It catalyzes the reversible transfer of the phosphoryl group from phosphocreatine to adenosine diphosphate, to regenerate adenosine triphosphate (ATP) [1]. CK has two polypeptide chains of M and B and three isomers of CK-BB, CK-MB and CK-MM. B chain is specific for brain tissue and M chain is specific for muscle tissue. CK is present in the blood in small amounts and it exists at high levels in cells with high energy requirements such as skeletal, cardiac and smooth muscles, it is also found in kidneys, brain, neuronal tissues, retinal photoreceptor cells, spermatozoa and sensory hair cells of the inner ear [2-4]. Although physiologic rise in CK activity has been reported to be associated with muscle activity and exercise yet some disorders such as myocardial necrosis, acute skeletal muscle atrophy, muscular dystrophy, burns, epilepsy, surgical procedures, streptococcus postpartum infection, Streptococcal toxic shock syndrome also result in an increase in CK activity [5-7].

During labour, maternal serum CK activity show a several fold rise [8,9]. Surgical intervention during labour further increases the activity of CK in the serum. Several studies demonstrated different changes in CK activity during labour and its association with the type of delivery. It has been shown that maternal and cord blood CK activity are higher in cesarean as compared to normal delivery [10-12]. Pharmacological agents such as cocaine, ethanol and halothane are other factors responsible for increased CK activity [13]. Brain damage, low birth weight, term of delivery and skeletal injuries during delivery could be related to higher CK activity in cord blood [14]. Persistent high activity may implicate some conditions such as rhabdomyolysis and significant brain injuries [15-18].

Considering the fact that cord blood activity of Creatine kinase might characterize the different prenatal events. Measuring the CK activity in the cord blood and then analyzing them with various parameters will help to assess its correlation with different perinatal events such as mode of delivery and APGAR score.

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Oobjective: Our study aimed to correlate total CK activity with mode of delivery and APGAR score.

METHODOLOGY

Study was conducted in the department of Obstetrics and Gynecology, and Biochemistry, Era's Lucknow Medical College and Hospital, Lucknow. Cord blood of 100 full term newborns was collected and Serum was analyzed for total CK activity by modified IFCC method.

After obtaining history of mother and previous offsprings, the informed consent was taken from parents and 3ml cord blood samples of study participants were collected in a plain vial. Serum was used to estimate the total CK activity. Data about at birth and 5 minutes APGAR scores, gender, birth weight , mode of delivery were also recorded

Inclusion and exclusion criteria

Cord blood samples were collected from the newborn babies born at gestational age 37-42 weeks, having birth weight (≥ 2.5 kgs), while the samples from Preterm and post-term babies, newborns with any congenital malformation and low birth weight newborns were excluded.

Estimation of Creatine Kinase activity

Total CK activity was measured by modified IFCC method on semii-autoanalyser by immunoinhibition method. Technical bulletin supplied along with the kit was followed.

Ethical issues

Ethical clearance and permission for study was obtained from the Institutional Ethical Committee, Era's Lucknow Medical College, Lucknow. Informed consent was obtained from the parent/guardians of the newborns. Confidentiality regarding sample collection and new born's information was maintained.

Study Design

Prospective observational study.

Data processing and analysis

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 18.0 statistical Analysis Software. Cross-tabulations were generated, and comparisons were made, significance was considered at p-value of less than 0.05

RESULTS

Out of 100 newborns, 51 were delivered by full term normal vaginal delivery (FTND) and 49 by lower segment cesarean section (LSCS) [Table1]. Maximum mothers were in the age group of 21 to 30 years [Table 2]. Majority of babies enrolled in the study were males (60%). There were 40 (40%) females. Male to female ratio was 1.5:1 [Fig 1]. Birth weight of the babies ranged between 2.5 to 3.7 kg. Most of the newborns had birth weight in range 2.5-3.0 kg (74%) followed by those having birth weight 3.1-3.5 kg (21%) and >3.5 kg (5%) respectively. Mean birth weight of babies was 2.89 ± 0.33 kg [Fig 2].

Table 1: Distribution according to mode of Delivery

	Mode of Delivery	No. & %
1.	Vaginal	51
2.	LSCS	49

Table 2: Distribution of cases according to Maternal Age

Maternal Age	No. & %
≤20 Years	5
21-25 Years	47
26-30 Years	39
31-35 Years	7
36-40 Years	2
Mean Age ± SD	26.14 ± 3.97

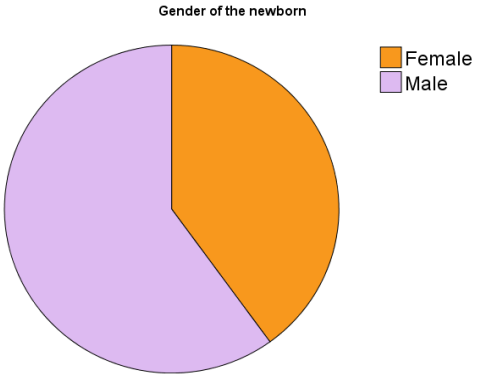

Figure 1: Percentage distribution of cases according to gender of newborn

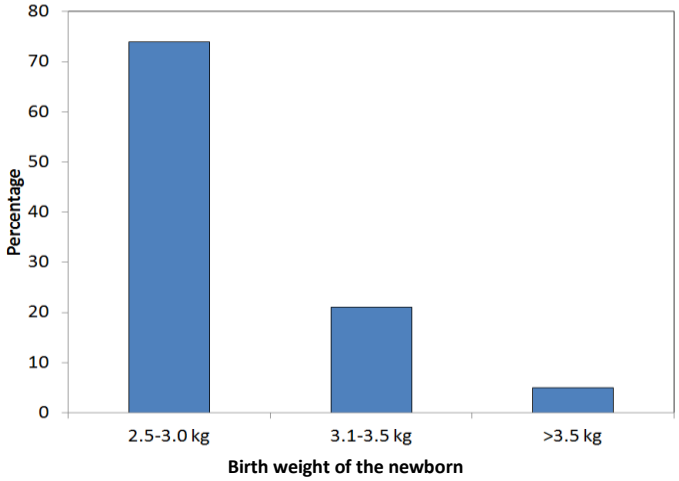

Figure 2: Distribution of cases according to birth weight

Data about at birth and 5 minutes APGAR scores were also recorded. At 1 minute, a total of 8% had APGAR score <7, 20% had APGAR score 7 and 72% had APGAR score >7. At 5 minutes, a total of 3% had APGAR score <7, 2% had APGAR score 7 and 95% had APGAR score >7. [Fig 3].

Cord blood Total creatine kinase activity ranged from 65.59 to 327.00 U/L with a mean of 146.20 and a standard deviation of 45.79. [Table 3]. Mean total CK activity was significantly higher ($p<0.001$) among cases born through cesarean section as compared to those born vaginally [Table 4]. With increasing APGAR scores a significant decline in Total CK activity was observed ($p<0.001$) at both 1 minute and 5 minutes [Table 5 and 6]. Mean Total CK activity was recorded maximum in age group ≤20 years and minimum in age group 36-40 years yet the association of Total CK activity with maternal age was not significant ($p=0.982$) [Table 7]. Gender-wise no significant difference was observed for total CK activity ($p=0.748$) [Table 8].

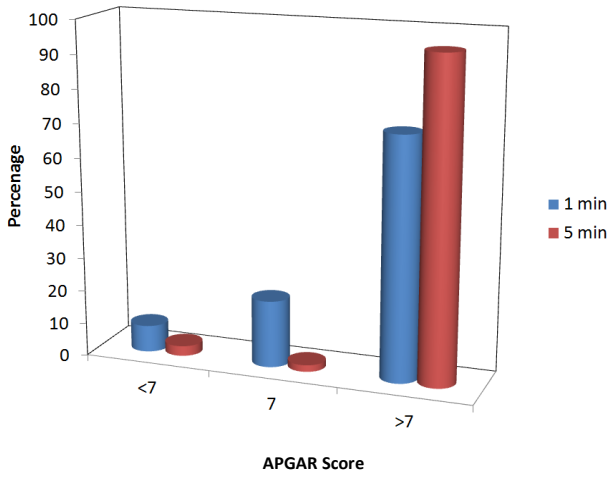

Figure 3: Percentage distribution of cases according to APGAR Score

Table 3: Total CK activity (U/L) in cord blood of neonate

	N	Minimum	Maximum	Mean	Std. Deviation
Total CK activity	100	65.59	327.00	146.20	45.79

Table 4: Association of Total CK activity (U/L) with mode of delivery

Mode	No.	Total CK (Mean±SD)
Vaginal	51	131.89±31.12
LSCS	49	162.33±54.01
't'		3.501
'p'		0.001

Table 5: Association of Total CK activity (U/L) with 1 min APGAR score

APGAR at 1 min	No.	Total CK (Mean±SD)
<7	8	215.58±57.71
7	20	160.12±29.05
>7	72	134.62±40.46
't'		16.22
'p'		<0.001

Table 6: Association of Total CK activity (U/L) with 5 min APGAR score

APGAR at 5min	No.	Total CK (Mean±SD)
≤7	5	227.42±65.40
8	12	175.09±37.19
9	83	137.13±39.11
't'		15.32
'p'		<0.001

Table 7: Association of Total CK activity (U/L) with maternal age

Maternal Age	No.	Total CK (Mean±SD)
≤20 Years	5	149.27±43.03
21-25 Years	47	144.70±44.27
26-30 Years	39	149.07±50.35
31-35 Years	7	141.02±36.06
36-40 Years	2	135.91±70.85
ANOVA (F)		0.100
'p'		0.982

Table 8: Association of Total CK activity (U/L) with gender of newborn

Gender	No.	Total CK (Mean±SD)
Male	60	144.99±48.42
Female	40	148.01±42.09
't'		0.322
'p'		0.748

DISCUSSION

Birth is an event that involves strenuous muscular activity, both for the mother and the neonate, as a result the creatine kinase levels are expected to be dependent on the level of strenuous activity or stressful events during the perinatal period. Studies have shown that at birth cord blood creatine kinase activity is raised [19], and thus as such some researchers believe it to be associated with pronounced muscular activity associated with birth [20]. Pregnancy events are affected by a number of factors that ultimately determine the level of risk for a fetus and/or mother.

In present study, we found the maternal age of 5 neonates to be in teenage range (≤20 years) and 9 to be in advanced age (>30 years) and thus maternal age as a surrogate risk factor was noticed in these 14 cases. However, the data analysis revealed that there is no effect of age on Total-CK activity. In fact, our hypothesis that early pregnancy and late pregnancy, which are considered to be high risk pregnancies which affect the perinatal outcome, might influence the perinatal stress and in turn creatine kinase activity seems to have no statistical outcome, however, we would like to mention here that the total CK activity were found to be maximum in cord blood of those neonates whose maternal age was ≤20 years and despite our inability to produce a statistically proven association these relationships worth further examination in larger trials.

Most of the neonates under study were males (60%). The higher proportion of males as compared to female (1.5:1) in present study could be incidental as well as dependent on selective practices of gender determination. An assessment was also made to evaluate the effect of neonatal sex on cord blood total CK and its isoenzymes, however, we failed to deduce any such relationship. Very few studies are available showing an insignificant association between CK activity and sex. In present study, all the neonates were ≥2.5 kg of weight which was primarily in accordance with the inclusion criteria of the study. The fact that the present study used a sampling frame which ruled out recording of all the consecutive deliveries and focused on the selection of only those neonates who were born at term, had a birth weight ≥2.5 kg and did not have any congenital anomalies might have also ended up in the deviation of gender and cesarean section delivery rates in present study.

Mode of delivery can be termed to affect the level of stress during labour and delivery, thus can affect the maternal and fetal endocrinal response [21]. On the other hand, fetal distress is a known indication for cesarean delivery [22,23] which might in turn affect the muscular activity and thus creatine kinase activity. In the present study, a total of 49 out of 100 neonates were born through cesarean section. The proportion of neonates born through normal vaginal delivery was relatively higher. According to WHO in 2008, the cesarean rate stands at 8.5% in India [24], however, it is showing an incremental trend throughout the world including India [25]. A high cesarean rate in present study could purely be incidental because of the limitations of inclusion and exclusion criteria. It was observed that mean total CK activity was significantly higher in cesarean deliveries as compared to vaginal deliveries. Similar to results of present study Sakha and co-researchers observed that CK activity was higher in neonates delivered via Cesarean section and this difference was meaningful in Cesarean section with labor pain in comparison to vaginal delivery. As a whole there was a meaningful difference between Cesarean section and vaginal delivery, but no

difference was found between elective and Cesarean section with labor pain. What could be the reason for these varying responses in different studies? Sakha and workers [26] explained that the alteration in creatine kinase activity might be dependent on type of anesthesia and/or mother tissue injury by surgical procedure. In our study, same could be the reason for raised Total CK activity in Cesarean section mode of delivery.

In our study, we also observed a significant decrease in total CK activity with increasing APGAR scores (both 1 min as well as 5 min). This finding is in agreement with the observations made by several studies who have found a significant association between asphyxia and increased total CK activity [26-28].

CONCLUSION

Mean total CK activity was significantly higher in neonates delivered through LSCS delivery as compared to those delivered through vaginal delivery. No significant association of total CK activity was observed with maternal age and gender of neonate. Mean total CK activity showed a significant incremental trend with decreasing APGAR scores at 1 and 5 minutes.

Conflict of Interest

Authors declare no conflict of interest.

Author's Contribution

Asfia Khan : Literature search, Sample collection and investigation and data compilation. Brijesh Rathore : Manuscript preparation Kanchan Singh, Shitanshu Shrivastava : Concept of study Aparna Misra, Shipra Kunwar : Data analysis.

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