ORIGINAL ARTICLES

DIAGNOSTIC ACCURACY OF PLASMA LACTATE IN NEONATAL BIRTH ASPHYXIA

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ABSTRACT

Objective: To find out the diagnostic accuracy of levels of plasma lactate in neonatal birth asphyxia by taking pH as gold standard.

Study Design: Cross sectional validation study.

Place and Duration of Study: The study was conducted at Paediatrics Department, Pak Emirates Military Hospital Rawalpindi, from May to Nov 2013.

Material and Methods: Two Hundred and forty neonates were selected through non-probability purposive sampling after informed consent from parents by inclusion and exclusion criteria. The sample size was calculated by WHO calculator. The plasma lactate and pH of the neonates were taken within first six hours of delivery of child. The samples were sent in heparinized containers along with ice packs and were stored at 0°C to -2°C.

Results: Gestational age of 52.5% (n=126) neonates was between 34-37 weeks while 47.5% (n=114) was between 38-40 weeks with a mean of 37.75 ± 2.91 weeks. Gender distribution among neonates showed that 58.75% (n=141) male and 41.25% (n=99) females. The diagnostic accuracy of plasma lactate in neonatal birth asphyxia by taking pH as gold standard showed 194 (80.83%) true positive, 7 (2.92%) false positive, 31 (12.92%) true negative and 8 (3.33%) were false negative. The test has sensitivity = 96.04%, specificity = 81.58%, positive predictive value= 96.52%, negative predictive value = 81.58% and accuracy of 93.75%.

Conclusion: There was a higher diagnostic accuracy of plasma lactate by taking pH as gold standard for the diagnosis of neonatal birth asphyxia.

Keywords: Diagnostic accuracy, Neonatal birth asphyxia, Plasma lactate.

INTRODUCTION

A study conducted in India has shown that the prevalence of birth asphyxia is 18.1%[1]. Most common cause of neonatal morbidity and mortality is birth asphyxia[2]. Definition of birth asphyxia is "the failure to initiate and sustain breathing at birth" by World Health Organization[13]. There is an estimate by World Health Organization (WHO) that about 8 to 9 million neonates suffer from the birth asphyxia annually. There is a death of around 1.2 million neonates after the birth asphyxia. There is almost same number of neonates who survive the episode of birth asphyxia, have a poor neuro-developmental outcome[2,3]. Birth asphyxia is a cause of about 29% of the neonatal deaths as per World Health Organization (WHO) statistics. This results to a considerable load of long term neurological disability and impairment[4].

Lack of oxygen supply to the body organs is called Perinatal asphyxia which can occur immediately before, during or after delivery[5]. Antepartum factors result in about 20 percent of cases[5,6] thirty five percent due to Intrapartum events[5-7] and postnatal insults in approximately 10 percent cases whereas in 35 percent cases the cause is intrauterine growth retardation[7].

A lot of problems are associated with perinatal asphyxia. These include central nervous system dysfunction, congestive heart failure, cardiogenic shock, persistent pulmonary hypertension, respiratory distress syndrome and gastro intestinal perforations[8] other conditions such as prematurity and congenital anomalies can also

obstruct the initiation of adequate breathing at birth and consequently oxygen supply to the body resulting in perinatal asphyxia at later stages[5,6,9].

Outcome of perinatal asphyxia can be altered by timely diagnosis and resuscitation. It is vital to look for helpful predictors early in the course of the disease, preferably within the first 6 hours after birth like APGAR score, pH of the blood and plasma lactate levels[10].

Predictive value of pH, and lactate for the occurrence of hypoxia was compared by Shah *et al*[8] and the study found that the plasma lactate has sensitivity of 94% and specificity of 67%. Whereas the gold standard for diagnosis of hypoxic ischemic encephalopathy is low arterial pH along with clinical evidence of low APGAR score. This has sensitivity 96% and specificity 98%[8].

This study was designed to find out the diagnostic accuracy of plasma lactate in patients of asphyxia by taking pH as gold standard. A considerable number of deaths occur along with severe disabling neurological complications because of birth asphyxia. Therefore, reliable and sensitive investigations are required to be identified to minimize the mortality and morbidity associated with birth asphyxia.

MATERIAL AND METHODS

This cross-sectional validation study was conducted at the Paediatrics Department, Pak Emirates Military Hospital, Rawalpindi, a tertiary care hospital. Duration of study was six months from 05 May to 05 November 2013. Sample size was calculated using World Health Organization (WHO) Calculator by taking sensitivity of 94% and 67%, prevalence of 18.1% and precision of 6% and 10% with 9% confidence interval. Total sample size was 240 neonates. Samples were selected through non-probability purposive sampling. Neonates with APGAR score less than 3 at 1 and 5 minutes, gestational age greater than 34 weeks and birth weight greater than 2000 grams were included in the study. Whereas the neonates with life threatening congenital malformations, chromo-somal abnormalities like

trisomy 13, 18 and 21, congenital hydrocephalus, trauma like cephalo-hematoma, sub aponeurotic hemorrhage and caput succedaneum, Pulmonary disease like respiratory distress syndrome were excluded from the study.

Study was commenced after taking informed consent from parents of neonates. Information regarding gestational age, prenatal history and birth history was obtained from the parents. Plasma lactate and pH of the neonates were sent to Armed Forces Institute of Pathology (AFIP), Rawalpindi in heparinized sample bottles along with ice packs. The samples were stored at 0°C to -2°C. Tests were analyzed within six hours of

+	pH	-
True positive (a)	False positive (b)	
False Negative (c)	True Negative (d)	
+	Plasma Lactate	-

Sensitivity = a / a+c x 100, Specificity = d / b+d x 100, Positive predictive value = a / a+b x 100, Negative predictive value = d / c+d x 100, Diagnostic accuracy = a + d / a + b + c + d x 100

delivery via IGI - 13100 Philips gas analyzer and were reported by a classified pathologist.

Data was entered in predesigned structured proforma. Data was analyzed by statistical software version SPSS version 18. Quantitative data like gestational age and baby's weight was analyzed by calculating mean and standard deviation. Qualitative data like sex, and true positive cases was analyzed by calculating frequency and percentages. 2x2 tables was prepared to find out the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of plasma lactate by taking pH as gold standard. Birth asphyxia was confirmed by blood pH to be less than 7. A plasma lactate concentration higher than 3.6 mmol/L within first 6 hours of delivery was considered as increased lactate levels whereas level below 3.6 mmol/l were considered normal. The percentage of patients with increased lactate levels and acidic Ph were taken as true positive cases. The percentage of patients with normal plasma lactate levels and normal pH were taken as true negative. The percentage of patient diagnosed as having birth asphyxia by increased level of

plasma lactate and normal pH were taken as false positive cases. Whereas the false negative cases were the percentage of patients having birth asphyxia diagnosed on normal levels of plasma lactate and acidic pH. Data was expressed by using tables.

RESULTS

A total of 240 cases fulfilling the inclusion and exclusion criteria were enrolled in the study

Diagnostic accuracy of plasma lactate in neonatal birth asphyxia by taking pH as gold standard was calculated, where True positive were noted as 194 (80.83%), false positive 7 (2.92%), true negative 31 (12.92%) and false negative were 8 (3.33%), whereas sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate were calculated as 81.58%, 96.52%, 81.58% and 93.75% respectively (table-II).

Table-I: Gestational age, gender distribution and mean weight of neonates (n=240).

Age (in weeks) (37.75 ± 2.91)	No. of patients	Percentage
34-37	126	52.5
38-40	114	47.5
Gender Distribution		
Male	141	58.75
Female	99	41.25
Mean Weight (grams)	Mean	S.D
	2350.238	161.73

Table-II: Diagnostic accuracy of plasma lactate in neonatal birth asphyxia by taking pH as gold standard (n=240).

| Plasma lactate | Gold standard | | Total |
	Birth asphyxia (pH Decreased)	Birth asphyxia (pH Normal/Increased)	
Increased	True positive(a) 194 (80.83%)	False positive (b) 7 (2.92%)	a + b 201 (87.75%)
Normal	False negative(c) 8 (3.33%)	True negative (d) 31 (12.92%)	c + d 39 (16.25%)
Total	a + c 202 (84.17)	B + d 38 (15.83%)	240 (100%)

Sensitivity =a / (a + c) x 100 =96.04%, Specificity = d / (d + b) x 100 = 81.58%, Positive predictive value = a / (a + b) x 100 =96.52%, Negative predictive value = d / (d + c) x 100 =81.58%, Accuracy rate = a + d / (a + d + b + c) x 100 =93.75%

to determine the diagnostic accuracy of plasma lactate in neonatal birth asphyxia by taking pH as gold standard.

Mean Gestational age of the subjects was 37.75 ± 2.91 weeks, 52.5% (n=126) of neonates were between 34-37 weeks while 47.5% (n=114) neonates were between 38-40 weeks of gestation (table-I). Mean weight of the neonates was 2350.238 ± 161.73 grams. Gender distribution among neonates shows that 58.75% (n=141) males and 41.25% (n=99) females (table-I).

DISCUSSION

Birth asphyxia is a global problem for the neonatologists. It leads to serious sequelae with regards to neonatal mortality and morbidity[12]. Social, educational and economical standards of a community are reflected by its perinatal and neonatal mortality and birth asphyxia is a leading cause of this. 98% of approximately one million neonatal deaths occurring due to birth asphyxia are reported from the low and low middle income countries (LMIC)[15]. There are varying effects of birth asphyxia on the neonatal brain.

This depends upon the gestational age of the baby and the severity and time of onset of the asphyxiating event(s). The asphyxiating event can occur at any point in the infant's antepartum, intrapartum and postpartum life. Various neuro-developmental outcomes develop in neonates surviving the birth asphyxia like learning problems, intellectual disability and cerebral palsy[16-18]. Forty one million disability adjusted life years are caused by birth asphyxia making this as one of the top causes of neonatal morbidity and mortality in the low middle income coun-tries. Neonatal asphyxia requires immediate resuscitation at birth. About 6-10 percent of all neonates require some sort of intervention to initiate and establish normal breathing. Neo-natal mortality and morbidity can be decreased effective by timely apprehending and managing the neonatal birth asphyxia and initiating the resuscitation timely and effectively. As the survivors who survive the birth asphyxia live with some sort of disability. These children add a considerable burden on the health care system in a resource deficient countries. They also have low quality of life of the survivor neonates. Although, hypoxicischemic encephalopathy (HIE) is the hallmark of severe asphyxia, such cases can often exhibit multisystem failure involving the heart, kidneys and gastrointestinal systems. This in itself may pose difficult problems whereby optimal treatment of one system, e.g., volume expansion, may adversely affect another, e.g. acute renal failure.

This study was planned to find out the diagnostic accuracy of plasma lactate in patients of asphyxia by taking pH as gold standard. Birth asphyxia leads to a significant number of deaths and severe neurological complications. Therefore, reliable and sensitive investigations are required to be identified to minimize the mortality and morbidity associated with birth asphyxia.

Our findings are close to the findings of Shah et al[9] who compared the predictive value of pH, and lactate for the occurrence of hypoxia and found the sensitivity of 94% and specificity of 67% of plasma lactate.

It was predicted in a study that in neonates with severe hypoxemia requiring extracorporeal membrane oxygenation, plasma lactate values above 15 mmol/l lead to death by Cheung et al[11]. It was also recently recognized that plasma lac-tate values above 15 mmol/l predict unfavor-able developmental outcome in survivors with severe hypoxemia[11]. This has shown the impor-tance of plasma lactate in predicting birth asphyxia and its prognosis; however, the levels of plasma lactate were not used to predict the neonatal mortality.

There is very limited data available analy-zing diagnostic accuracy of plasma lactate in neonatal birth asphyxia. There is requirement of further studies to authenticate the findings of current study, so that the morbidity may be identified to minimize the mortality and morbi-dity associated with birth asphyxia.

CONCLUSION

The study concluded about a higher diag-nostic accuracy of plasma lactate by taking pH as gold standard for the diagnosis of neonatal birth asphyxia. But to establish these findings on a solid ground a larger multi-centric study is needed.

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CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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