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Original Article

The frequency of deranged coagulation profile in newborns with birth asphyxia.

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Abstract

Background: Birth asphyxia, a burdening pathology, is responsible for a great number of neonatal deaths. Besides targeting vital organs of the body, the associated systemic oxygen deprivation is responsible for the hemodynamic rearrangement and, consequently, the development of various coagulopathies. The present study is aimed to assess the alteration in the coagulation profile of babies born with birth asphyxia.

Methodology: A six-month cross-sectional research on newborns (with a gestational age of 30 to 42 weeks and birth asphyxia) was conducted in a hospital setting. A total of 96 newborns meeting the inclusion criteria were considered for the study. The blood samples were collected for the determination of prothrombin time (PT), activated partial thromboplastin time (APTT), and international normalized ratio (INR).

Results: The studied cohort comprised 54 (54.2%) females, and the mean age of the newborns was 12.53 ± 3.58 hours. The mean PT and APTT in the asphyxic newborns were 22.58 ± 10.22 and 37.67 ±10.25 seconds, respectively, while the INR was 2.12 ± 0.96. The deranged PT and APTT were observed in 60 (62.5%) and 32 (33.3%) newborns. The deranged INR was observed in 21 (21.9%). Further, the maternal use of antiepileptics and anticoagulant drugs was not traced in any studied subjects.

Conclusion: A significant number of newborns with birth asphyxia presented with a deranged coagulation profile. However, the maximum frequency for derangement was obtained for the PT, followed by the APTT.

Keywords

Newborns, Birth Asphyxia, Deranged Coagulation Profile, Prothrombin Time.

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Introduction

Birth asphyxia (BA) refers to the impairment of gaseous exchange due to the disruption in blood flow to the placenta. Consequently, there is the development of hypoxia, ischemia, and hypercapnia[1]. The World Health Organization (WHO) classically defines birth asphyxia as the failure to initiate, establish and sustain breathing at birth[2]. The past years have witnessed a persistent decline in child mortality, but in contrast, a stagnant trend has been observed for neonatal deaths[3].

Birth asphyxia is the third leading cause of neonatal mortality, accounting for ~24% of neonatal deaths after preterm births and life-threatening infections[4,5]. Further, the effects are not limited to death; BA is also responsible for various short-term and detrimental long-term severe neurological squeals, for instance, motor and cognitive disabilities, cerebral palsy, epilepsy, mental retardation, and neurodevelopmental disorders in the survivors, which are more often untreatable[6,7]. Besides the nervous system, BA affects almost every organ system, whereas pulmonary, renal, hepatic, cardiovascular, and hematological systems are among the common ones[8].

The hematological insufficiencies, for instance, coagulopathies, are more frequent in the neonatal period compared to any other life phase of the healthy subjects. During normal physiological conditions, the hemostasis is maintained to counter any increased risk of thrombosis or hemorrhage[9]. However, high-risk conditions such as asphyxic insult lead to hemostatic alterations resulting from platelets or liver dysfunctions or may be due to the derangement in the coagulation cascade[10,11].

The initial records of coagulation dysfunction date back to 1971 in neonates with BA, with the cause associated with a consumptive coagulopathy followed by disseminated intravascular coagulation[12]. It is noteworthy that experimental findings indicated that hypoxic conditions alone, without any alteration in PH, carbon dioxide, and blood pressure, do not disrupt the coagulation system to a greater extent. Nevertheless, variable proportions of all these components trigger the malfunctioning of the coagulation mechanism[13].

Information on coagulation status before the occurrence of clinical bleeding may possibility guide medical practitioners for early therapeutic interventions and to prevent detrimental outcomes The commonly used parameters to quantity in vivo coagulation rely on the coagulation's cascade model, i.e., the activated partial thromboplastin time (APTT) and the international normalized ratio (INR) an indicator of the prothrombin time (PT)[14,15]. In the past, only a few studies documented the status of the coagulation profile in asphyxiated newborns. In this regard, the present investigation aims to study the coagulation profiles of neonates with birth asphyxia. Since the variables/factors considered herein (PT, APTT, INR) are associated with bleeding, the present study can provide valuable information in devising future interventions.

Methodology

A cross-sectional study was performed from July 2021 to December 2021 at the NICU of a Pediatric Ward, Civil Hospital, Karachi-Pakistan. Before conducting the study, approval was acquired from the institutional ethics committee of Dow University of Health Sciences. The sample size was calculated following the assumption of non-probability consecutive sampling with the prevalence of deranged coagulation profile in asphyxiated newborns at 55%[13].

The inclusion criteria for the present study were newborns with asphyxia between the gestational age of 30 to 42 weeks, as confirmed via ultrasound scan or LMP. Further determinants included APGAR scores of ≤ 3 and 7 at one and five minutes after birth, respectively, or history of delayed cry, cyanosis upon physical examination, and resuscitation at birth where the APGAR score was not mentioned. At the same time, the exclusion criteria included the babies born with congenital abnormalities, for instance, microcephaly, hydrocephalus, meningomyelocele, cyanotic heart diseases, or those who develop bleeding within 6

hours since birth were excluded from the study. Furthermore, the patients with sepsis and hemorrhagic disease were also not considered.

Prior to the study, informed consent from all parent subjects fulfilling/meeting the inclusion criteria was acquired. The blood was collected for calculating PT, APTT, and INR in specially designed tubes provided by the central lab of the hospital. The PT APTT and INR of greater than 15, 40, and 1.5, respectively, were taken as prolonged for further management, and the outcome variable was recorded as deranged. Data were entered and analyzed using SPSS statistical package version 21.0. Per the data distribution, descriptive statistics, i.e., Mean and standard deviation, were calculated for numerical variables, including age and estimated values of PT, APTT, and INR. Frequencies and percentages were estimated for the qualitative variables like gender categories of PT, APTT, and INR, deranged coagulation profile, and status of birth asphyxia. The association between demographic variables (age and gender) and outcome variables (deranged PT, APTT, and INR) was assessed via the Chi-square test/$\chi 2$ test. The P value of <0.05 was considered statistically significant.

Results

During the study period of six months, a total of 96 newborns fulfilled the inclusion criteria. The mean age of the studied population was 12.53 ± 3.58 hours, comprising 52 (54.2%) females and 44 (45.8%) males. The gestational age vise categorization of the subjects revealed that 53 (55.2%) of the newborns were ≤12 hours, while 43 (44.8%) with >12 hours of age. The minimum age was 3, while the maximum age recorded was 23 hours (Table 1).

Table 1: Categorization of newborns based on gender and age.

Variables		n(%)
Gender	Male	44(45.80)
	Females	52(54.20)
Age Groups	≤12 hours	61(55.20)
	>12 hours	35(35.80)

When calculated, the mean PT of the newborns was 22.58 ± 0.22 seconds, whereas 60 (62.5%) newborns were presented with deranged PT. Similarly, the mean APTT was calculated and found to be 37.67 ± 10.25 seconds. The deranged APTT level was observed in 32 (33.3%) newborns. Further, the mean INR of the patients was 2.12 ± 0.96, while 21 (21.9%) newborns exhibited deranged levels upon investigation. (Figure 1). The description of the tested variables is mentioned in Table 2. Considering the tested variables, i.e., PT, APTT, and INR, the deranged coagulation profile was observed in 60 (62.5%) newborns.

Table 2: The descriptive statistics of the studied variables involved in the coagulation cascade.

Variables	Mean±SD
PT level (in seconds)	22.58±10.22
APTT level (in seconds)	37.67±10.25
INR (Ratio)	2.12±0.96

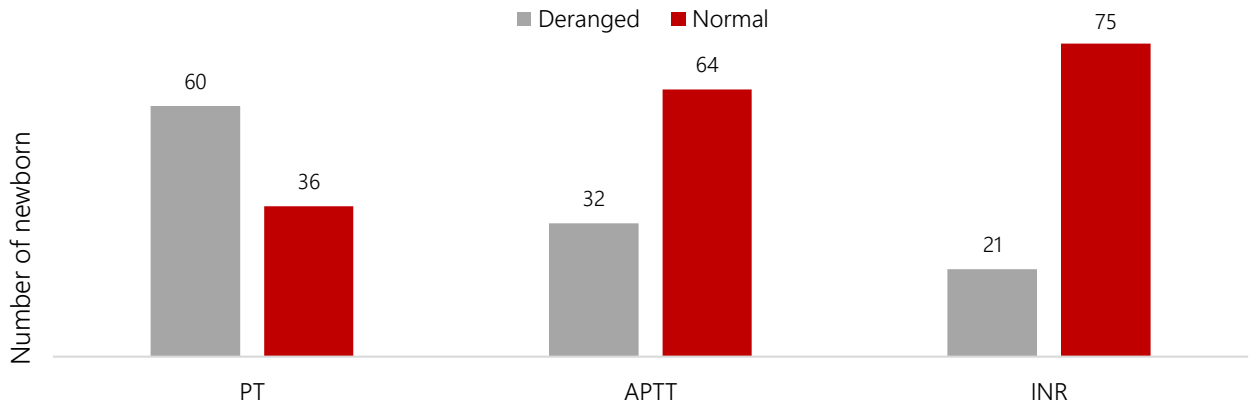

Figure 1: Coagulation profile of studied newborns.

The association between the demographics of the newborns and the PT, APTT, and INR, along with the overall deranged coagulation profile, is depicted in Table 3. The clinical history of the mother was also reviewed, and it was observed that none of the newborns had a history of maternal use of anticoagulant drugs and antiepileptics.

Table 3: Association of PT, APTT level, and INR demographic characteristics.

Variables	PT			APTT			INR		
	Deranged	Normal	p-value	Deranged	Normal	p-value	Deranged	Normal	p-value
Age									
≤12 hours	33(62.3)	20(37.7)	0.96	17(32.1)	36(67.9)	0.77	42(79.2)	11 (20.8)	0.77
>12 hours	16(37.2)	27(62.8)		15(34.9)	28(65.1)		33(76.7)	10(23.3)	
Gender									
Male	31(59.6)	21(40.4)	0.53	22(42.3)	30(57.7)	0.04*	9(17.3)	43(82.7)	0.24
Female	29(65.9)	15(34.1)		10(22.7)	34(77.3)		12(27.3)	32(72.7)	

*p-value < 0.05 is considered statistically significant.

Discussion

Birth asphyxia still accounts for most neonatal deaths worldwide, particularly in resource-limited settings[16,17]. The advancement in neonatal care has identified various strategies to resuscitate babies with such ailments to avoid devastating consequences. It is evident from the studies that compared to normal newborns, those with exposure to asphyxial insult are at higher risk of developing disseminated intravascular coagulation. The alteration in coagulation function is usually manifested with prolonged bleeding[15]. Thus, understanding the association of coagulation abnormalities with asphyxia may reveal new targets that can be exploited to prevent bleeding and, consequently, for future lifesaving interventions.

In this regard, the present study was designed to study the coagulation status of asphyxiated newborns. It was observed that more than half (62.5%) of the studied cohort presented with a deranged coagulation profile. It is further supported by the study by Go and colleagues (2019), who stated birth asphyxia is the leading risk factor for coagulation disorder[18]. Similar to our findings in patients suffering from hypoxic-ischemic encephalopathy, significant bleeding (53.9%) and deranged coagulation profile were observed[19]. Since Birth asphyxia triggers hemodynamic rearrangement, the diving reflexes ensure the blood supply to the more vital organs such as the brain and heart. In doing so, the supply to less vital organs, i.e., lungs, kidneys, Lungs, spleen, and liver, is compromised. The ischemic

conditions thus developed result in impaired physiological function affecting almost every tissue and organ[20].

In particular, the highest proportion of newborns presented with deranged PT (62.5%) levels, followed by APTT (33.0%) and INR (21.9%) in the studied cohort. Herein, no significant association was observed between gender and age and deranged factors, which may be attributed to the small sample size.

Similar to our study Ali and coworkers (2017) investigated the coagulation abnormalities and the early outcome in newborns with BA. It was found that maximum derangement was observed in fibrinogen level (59.3%) followed by PT (51.9%)[21]. Longer PT time was also noted by Michniewicz and colleagues (2020) in a studied cohort suffering from hypoxic-ischemic encephalopathy. The mean values of 17.0, 44.2, and 47.8, 47.9 s were recorded for PT and APTT in newborns categorized as moderate and severe HIE[22].

The PT and INR were also significantly higher in asphyxiated neonates. At the same time, Hypoproteinemia, along with prolonged PT and INR, was noted as the warning indicators of predicting mortality in a study conducted by Choudhary and coworkers[20].

A recent study in India also indicated that 55.1% of the neonates born with asphyxia presented with significantly higher PT and APTT compared to the respective control groups indicating the abnormal coagulation status[11].

Blood clotting is an ultimate effect of a complex series of events requiring less than 13 genes. Most coagulation proteins, i.e., factor X, VII, V, II, and I, are manufactured in the liver. The PT, APTT, and INR measure clotting factors and can actively detect substantial impairment; therefore serve as valuable biomarkers of liver function. Any alterations in these indices thus are directly correlated with liver dysfunction/ reflect hepatic dysfunction[15,20].

The present investigation was a pilot study and hence considered a small sample size; however, it can be extended to larger sample size to devise a more logical conclusion. Further, here the readings at a specific time were considered, and we can consider the multiple readings recorded at different periods. Thus, for future studies, we recommend increasing the sample size. Since the coagulation cascade involves an array of proteins thus, multiple factors other than those reported here should be considered.

Conclusion

Birth asphyxia is a well-known contributing factor to altering the hemostasis, bleeding, and clotting pathways. In the present work, the derangement in the coagulation profile was assessed. As documented, our work also endorses that the presence of asphyxic conditions alters the coagulation profile of the individual. In particular, the frequency of deranged PT was found to be higher, followed by APTT and INR. Such conditions must be given attention since, if not diagnosed earlier may lead to detrimental outcomes due to excessive bleeding.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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