Original paper

The Effect of Birth Asphyxia on the Coagulation Status in Neonates

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Abstract

Background: Birth asphyxia has multi system effect, which predisposes to coagulopathy by enhancing consumption of platelets & some clotting factors as a results of the associated sever hypoxemia, acidaemia & sepsis
Objective: To study the effects of birth asphyxia & perinatal events on the coagulation status of newborn infants.
Patients & Methods: Across sectional study was done on 27 neonates with birth asphyxia in AL-Zahraa teaching hospital in Najaf city from period of first of February 2012 to first of July 2012. Blood samples were collected from the neonates within the first 24 hrs. After birth and sent for investigations including PT, PTT, plasma fibrinogen and platelet count.
Results: The study showed statistically significant effect of birth asphyxia on platelet count especially in severely asphyxiated neonates with Apgar score of 0 – 3 at 5 min after birth (plat. Count < 100,000 per mm^3) in comparison to neonates with Apgar score of 4 – 6 at 5min after birth.
Infants who have very low birth wt. (i.e. <1500 gms) had significantly lower platelet count (< 100,000 per mm^3) than infants with birth wt.>1500 gms
Birth asphyxia had no significant effect on PT, PTT, or fibrinogen level. Other perinatal and prenatal variables examined as (sex, maternal hypertension, DM, mode of delivery gestational age) did not show any significant association with coagulation status.
Conclusion: Thrombocytopenia (plat. <100.000 per mm^3) is seen in neonates with Apger score (0-3) at 5 min. and in neonates with very low birth wt. <1500gms). No statistically significant relation between birth asphyxia and PT, PTT and plasma fibrinogen level.
Keywords: Birth asphyxia, Coagulation status in neonates

Introduction

World Health Organization defined birth asphyxia as the failure of a newborn to initiate & sustain spontaneous breathing at birth (WHO, 2007) [(1)]. Spontaneous coagulopathy occur more frequently in the neonatal period than any other time in healthy individuals because newborns especially those with perinatal asphyxia, sepsis, infants of mothers with preeclampsia, preterm & small for gestational age infants tend to experience hemostatic alterations resulting from hepatic or platelets dysfunctions, and or derangement in clotting factors .Birth asphyxia predisposes to coagulopathy by enhancing consumption of platelets & some clotting factors as a results of the associated sever hypoxemia, acidaemia & sepsis [(2)]. Some reports have shown that the level of vitamin K dependent coagulation factors are significantly lower in infants with birth asphyxia than healthy one [(3)] .However these abnormalities in the coagulation tests do not usually manifest with clinically evident bleeding. Bleeding & or thrombosis accentuate morbidity & neonatal mortality in this group of babies

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[4]. Early-onset thrombocytopenia (<72 hours) is most commonly associated with feto maternal conditions complicated by placental insufficiency and/or fetal hypoxia [5, 10]. Transient destructive thrombocytopenia develops in a large proportion of hypoxic newborns. Platelets in newborn demonstrate several activities, including hemostasis and maintaining integrity of blood vessels. Hemostasis of a neonate is a dynamic system that gradually evolves throughout gestation and early infancy. [6]

The newborn physiological status affects the risk for and the presence of acquired hemostatic disorders. Prematurity, birth asphyxia (BA) and small for gestational age (SGA) babies have been associated with hemostatic abnormalities. [7]

Patients and methods

Patients

This prospective study had been carried out at AL- Zahraa Teaching Hospital in AL –Najaf city from the first of February to the first of July 2012. The study was done on neonates suffering from birth asphyxia & were admitted to the NICU .written consent was obtained from the parents of the babies before enrollment into the study babies with birth asphyxia were those with APGAR score of less than 7 at five minutes after birth & didn't cry immediately after delivery[5].

Data from 27 newborn cases were diagnosed as having birth asphyxia based on the evaluation of the newborn condition which had necessitated emergency resuscitation with intubation and positive pressure ventilation in the resuscitation unite of the neonatal nursery unite after vaginal delivery or resuscitation of operative theater after cesarean section and depending on the Apgar score grading at first minutes then we categorized them either mild asphyxia from 4-6 or sever asphyxia from 0-3 that necessated admition to IPCU and neonatal nursery units.

All neonates didn't receive vitamin K prophylaxis.

Data Collection

A special question (appendix) had been designed to collect data about the following:

•Neonatal information regarding;

Neonatal name, age, weight, sex, gestational age, product of single or multiple gestation, mode of delivery, whether normal veginal delivery ,cesarean section or assisted labor, Apgar scor at the 1st min., 5min., and 10 min. after birth.

- Labor information .prolonged labor, induced labor, prolonged rupture of membrane, meconium stained amniotic fluid and mal presentation.
- Maternal information: age, medical diseases like DM, hypertension, infection, drug treatment, antenatal attendance and family history of bleeding tendency.

Method

Two blood samples were collected within the first 24 hour of labor from the peripheral veins in 2 tubes were labeled for the required tests and transported to the laboratory within less than half an hour of collection ,on arrival at laboratory the specimens were registered and one of them send to clotting units in which a 0.2 ml of sodium citrate put in plain tube and add 1.8 ml the blood sample from which will calculate the prothrombin time (PT) by exclude 0.1 ml of patients plasma and put it in small plastic tube incubated in digicllot apparatus (or water path) at 37C^ for 2 minutes then add 0.2 ml from prewarmed thromboplstin at least 15 mints simultaneously start a timer and record the clotting time (normal value 11-16 seconds).

Partial Thromboplastin time (PTT)

Calculated by taking 0.1ml of patients plasma in test tube and adding 0.1 ml of PTT reagent; that was prepared by dissolving in 2ml distilled water and putting digiclot (or water path) for 2 minutes and starting the stop watch with

the adding of 0.1 ml calcium carbonate and mix gently to observe the clotting time (normal value 25 -40 sec).

Plasma fibrinogen:

Calculated by putting of a0.9 ml of owerns veronal buffer in kahn tube and add 0.1ml of patient plasma to it and will take 0.2 ml from the mixture and putten in small test tube that will putten in water path at 37C for 2 minutes then will add 0.1 ml of diafibrinogen with simultaneous starting the stop watch with observing for clot formation by tilting method stopping the watch at first appearance of fibrin web then will plat the mean of the double determination son Dia -Med fibrinogen graph (normal value 160 -350 mg /dl).

The platelet count:

(2^{nd}) blood sample collected in EDTA tube and send to the hematological unit in the laboratory for assessment of platelet count by apparatus called system that automatically calculate the hematological and coagulation systems.

Assessment and follow up of patients:

All neonates were followed up during hospitalization for signs of bleeding tendency, other complications and outcome (discharged well, with sequels or death).

Data analysis

Data were fed into a computer and analyzed using SPSS 22(Chi-Square test), *P* values <0·05 were considered significant.

Results

A cross sectional study was done on 27 neonates with birth asphyxia (i.e. Apgar score <6 at first minutes after birth).

Fifteen (55.6%) neonates were males, 12(44.4%) neonates were female, and 12 (44.4%) neonates were of full term while 15 (55.6%) neonates were preterm.

All of the studied neonates had no family history of bleeding tendency except one with maternal history of antenatal treatment with anticoagulant drug for DVT disease.

Five (18.5%) neonates were product of normal vaginal delivery, while 22(81.5) of asphyxiated neonates were product of cesarean section.

All neonates didn't receive vit. K prophylaxis after birth.

There is statistically significant relation between platelet count and Apgar score as seen in table (1), also there is statistically significant relation between platelet count and VLBW as seen in table (2).

Table (3) shows the relation between coagulation profile and gestational age, table (4) shows the relation between coagulation profile and the sex of asphyxiated neonate, table (5) shows the relation between coagulation profile and the mode of delivery.

Table 1. Relation of coagulation profile to the apgar score at 5 minutes after birth

Coagulation profile Results		Apgar score at 5 min.		Total
		0-3	4-6	
PT	**normal**	9	4	13
	prolonged	10	4	14
	PV	0.16		
	normal	13	8	21
	prolonged	6	0	6
	PV	0.09		
Platelets	**normal**	8	8	16
	Decreased	11	0	11
	PV	0.03		
Fibrinogen	**Normal**	8	3	11
	Decreased	11	5	16
	PV	0.58		

Maternal risk factors as hypertension is seen in 5(18.5%) neonates, antenatal infection in 2(7.4%), diabetes mellitus in one (3.7%) and epilepsy in one (3.7%) neonates. The outcome of those asphyxiated neonates was death in 15 (55.6%) neonates and the remained 12 (44.4%) was alive and discharged well without complication.

Discussion

The purpose of this study was to investigate the coagulation status of infants with birth asphyxia and to assess the effect of abnormalities in coagulation on the early outcome of those infants.

Table 2. Relation of coagulation profile to the birth weight

Coagulation profile results		Birth weight (gms)				Total
		<1500	1500-2000	2001-2500	>2500	
PT	**normal**	1	3	2	7	13
	prolonged	4	4	1	5	14
	PV	0.18	0.54	0.47	0.35	
PTT	**normal**	3	6	3	9	21
	prolonged	2	1	0	3	6
	PV	0.49	0.49	0.45	0.55	
Platelets	**normal**	1	5	3	11	20
	Decreased	4	2	0	1	7
	PV	0.01	0.6	0.38	0.07	
Fibrinogen	**Normal**	2	2	2	5	11
	Decreased	3	5	1	7	16
	PV	0.68	0.38	0.35	0.61	

Table 3. Relation of coagulation profile to the Gestational age

Coagulation profile results		gestational age		Total
		preterm	Full term	
PT	**normal**	8	5	13
	prolonged	10	4	14
	PV	0.09		
PTT	**normal**	12	9	21
	prolonged	3	3	6
	PV	0.55		
Platelets	**normal**	8	11	19
	Decreased	7	1	8
	PV	0.08		
Fibrinogen	**Normal**	6	5	11
	Decreased	9	7	16
	PV	0.6		

Table 4. relation of coagulation profile to the sex of asphyxiated neonates

Coagulation profile results		sex		Total
		male	female	
PT	**normal**	10	3	13
	prolonged	5	9	14
	PV	0.07		
PTT	**normal**	12	9	11
	prolonged	13	3	16
	PV	0.55		
Platelets	**normal**	9	10	19
	Decreased	6	2	8
	PV	0.18		
Fibrinogen	**Normal**	7	4	11
	Decreased	8	8	16
	PV	0.4		

Table 5. Relation of coagulation profile to the mode of delivery of asphyxiated neonates

Coagulation profile results		Mode of delivery.		Total
		vaginal	C.S.	
PT	**normal**	2	11	13
	prolonged	3	11	14
	PV	0.53		
PTT	**normal**	3	18	21
	prolonged	2	4	6
	PV	0.3		
Platelets	**normal**	1	18	19
	Decreased	4	4	8
	PV	0.17		
Fibrinogen	**Normal**	2	9	11
	Decreased	3	13	16
	PV	0.68		

Our evaluation showed that there was no statistically significant difference between infants with Apgar score (0-3) at 5 mints. After birth and infants with Apgar score (4-6) at 5 mints after birth regarding PT, activated PTT and serum fibrinogen and also shows no statistically significant effect of birth asphyxia on PT, activated PTT and serum fibrinogen level Hemostasis of a neonate is a dynamic system that gradually evolves throughout gestation and early infancy [(6)]. The newborn physiological status affects the risk for and the presence of acquired hemostatic disorders. Prematurity, birth asphyxia (BA) and small for gestational age (SGA) babies have been associated with hemostatic abnormalities [(7)].

The study shows that the platelet count of neonates with Apgar score (0-3) at 5 mints after birth is significantly low (< 100,000 per mm^3) in comparison with neonates with Apgar score (4-6) at 5 mints after birth all has platelet count >100,000 per mm^3), similar result to our study was obtained by other studies [(8,9)].

The incidence of thrombocytopenia in the general neonatal population is low. In contrast, thrombocytopenia in the neonatal intensive care unit (NICU) is quite common [(1,10,11)].

Neonatal thrombocytopenia occurs more frequently in neonates with history of birth asphyxia than in non-asphyxiated neonates.

Our study shows that platelet count is affected by birth weight .neonate with birth weight < 1500 gms have significantly low platelet counts <100,000 per mm^3, [(12)] concluded that thrombocytopenic infants had a significantly lower birth weight. In another study conducted by Zaccheaus *et al*. [(13)] 13.6% of thrombocytopenic infants were of low birth weight. Hidehiko Maruyana *et al*. [(14)] concluded that birth weight and head circumference of the infants with thrombocytopenia were significantly smaller than those infants without thrombocytopenia.

The reduced number of platelet in SGA neonates' maybe the result of impaired thrombopoiesis due to the limited maturity of the organs responsible for this process. Thrombopoiesis in newborns occurs in liver and spleen. Hiett *et al*. found a lower number of hematopoietic progenitor cells in the cord blood of SGA when compared to AGA. -33[(15)]. This may indicate an impaired process of megakaryopoiesis.

Gestational age, sex and mode of delivery have no effect on platelet count of asphyxiated infants as shown in this study.

Hypoxia is an important aggravating risk factor in preterm for development of thrombocytopenia as compared to non-hypoxic term and preterm neonates [(16, 17)].

The present study confirms that plat. counts in infants with birth asphyxia are low which may further increase the vulnerability of the haemostatic system.

No one of asphyxiated neonates develop bleeding tendency.

Conclusion & Recommendations

1- We conclude that thrombocytopenia is a frequent association with asphyxia and is associated with very low birth weight.so we recommend Screening for development of thrombocytopenia is in hypoxic neonates & in very low birth weight neonates.)
2- No effect of birth asphyxia on PT. Activated PTT and serum fibrinogen level.
3-No one of the asphyxiated neonate develop bleeding tendency.

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