

## Original Article

# Dynamic observation on primitive fibrinogen and antithrombin III activity in premature infants

Peng Liu, Xiao-Li Zhang

*Pediatric Neonatal Intensive Care Unit, Shanxi Dayi Hospital, Taiyuan 030032, China*

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**Abstract:** Objective: To detect the changes of plasma fibrinogen and antithrombin III activity in premature infants of different gestational age and those with maternal pregnancy-induced hypertension (PIH) or not after birth, and discuss its clinical significance. Method: 51 premature infants with gestational age of less than 34 weeks and 45 premature infants of 34-37 weeks were selected. Based on whether their mothers had PIH or not, they were divided into PIH group (50 cases) and absent PIH group (46 cases), respectively. The plasma fibrinogen and antithrombin III activity were measured within 24 hours and on day 5 after birth, respectively. Results: The plasma fibrinogen and antithrombin III activity of premature infants within 24 hours and on day 5 after birth were at lower levels. The plasma fibrinogen and antithrombin III activity among premature infants with gestational age of less than 34 weeks were lower than those among premature infants of 34-37 weeks, with significant differences. Moreover, the plasma fibrinogen and antithrombin III activity of premature infants within 24 hours and on day 5 after birth among maternal PIH group were lower than those among absent PIH group, respectively, with significant differences ( $P < 0.05$ ). Conclusion: Dynamic detection of plasma fibrinogen and antithrombin III activity in premature infants after birth is significant to prevent hemorrhagic syndrome of premature infants, but its diagnostic value in disseminated intravascular coagulation remains to be further investigated.

**Keywords:** Neonate, premature infant, fibrinogen, antithrombin III, pregnancy induced hypertension, disseminated intravascular coagulation (DIC)

## Introduction

Neonates have different blood clotting and fibrinolytic activity from the adults, among which there are noticeable differences between premature and full-term infants [1, 2]. Compared with full-term infants, premature infants are more prone to bleeding diseases after birth, such as intracranial hemorrhage, pulmonary hemorrhage, hemorrhage of digestive tract, etc. The coagulation and anticoagulation system in vivo may partly explain the phenomenon. The lack of personal coagulation factors in premature infants and the influence from maternal pregnancy-induced hypertension (PIH) contribute to predisposition of bleeding in premature infants [2].

Fibrinogen (FIB), a glycoprotein synthesized and secreted by liver, is the most abundant blood coagulation factor in the plasma, which is hydrolyzed into fibrin by thrombin and plays an

important role in coagulation. Moreover, it is the main substance involved in the hemostasis and thrombosis. It is revealed that the level of FIB is significantly increased in pregnant women [3], especially in those with PIH, since hypertension could strengthen the coagulation and anticoagulation mechanism, making high coagulation status more obvious [4]. This research showed that FIB levels in premature infants of different gestational age were lower, and FIB levels in lower gestational age group and maternal PIH group were lower than those in higher gestational age and maternal absent PIH group, respectively. It is speculated that the finding above is related with immature liver development. As the increase of gestational age, FIB levels of premature infants are increased. On the other hand, it may be related to the high blood coagulation status of maternal PIH, but the specific mechanism of maternal high coagulation status affecting FIB levels in neonates is still unclear.

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**Table 1.** The results of fibrinogen and antithrombin III activity in premature infants with gestational age of less than 34 weeks ( $\bar{X} \pm SD$ )

Groups	Cases	Within 24 hours after birth		Day 5 after birth	
		FIB (g/L)	AT-III (%)	FIB (g/L)	AT-III (%)
Pregnancy induced hypertension group	21	1.06±0.46	32.90±10.97	1.34±0.36	35.81±12.07
Absent pregnancy induced hypertension group	30	1.53±0.84	38.24±11.59	1.68±0.32	42.38±10.00
t		1.124	1.260	1.481	1.892
P		<0.01	<0.05	<0.01	<0.05

**Table 2.** The results of fibrinogen and antithrombin III activity in premature infants with gestational age of 34-37 weeks ( $\bar{X} \pm SD$ )

Groups	Cases	Within 24 hours after birth		Day 5 after birth	
		FIB (g/L)	AT-III (%)	FIB (g/L)	AT-III (%)
Pregnancy induced hypertension group	25	1.13±3.82	31.20±7.98	1.43±2.90	34.20±6.48
Absent pregnancy induced hypertension group	20	1.21±3.20	40.69±7.94	1.53±3.41	41.91±9.44
t		1.340	2.334	1.678	2.269
P		<0.01	<0.05	<0.01	<0.05

Antithrombin III (AT-III), a single-chain glycoprotein secreted by liver and vascular endothelial cells, acts in anticoagulation regulation in human body [5], which is involved in maintaining the dynamic balance of the anticoagulation and coagulation system in vivo. Meanwhile, it is also a good indicator of high coagulation status [6]. The study showed that the activity of plasma AT-III in premature infants of different gestational age was at a lower level during early stage after birth. And the smaller the gestational age, the lower the activity of AT-III. The AT-III level in premature infants with maternal PIH was lower compared to those without maternal PIH. The possible reason may be that the premature infants themselves are at a lower coagulation status, therefore the anticoagulation and coagulation mechanism are at dynamic equilibrium of a lower level.

This study aimed to detect the changes of plasma fibrinogen and antithrombin III activity in premature infants of different gestational age and those with or without maternal PIH during pregnancy after birth, and discuss its clinical significance.

### Materials and methods

#### General information

**Subjects:** ① From January 2012 to April 2013, ninety six premature infants were selected in

our department, among which 51 cases were less than 34 weeks in gestational age. According to maternal PIH, they were divided into PIH group (21 cases) and absent PIH group (30 cases). There were 45 premature infants with gestational age of 34-37 weeks, which were divided into PIH group (25 cases) and absent PIH group (20 cases) according to maternal PIH during pregnancy or not. ② All the mothers in the two groups had no other complicated diseases during pregnancy, such as diabetes, thyroid disease, blood disease and infection, and asphyxia was absent for all the premature infants after birth.

#### Specimen collection

Two milliliter femoral venous blood was collected from premature infants within 24 hours and on day 5 after birth, respectively, and 0.5 mL sodium citrate was used against coagulation. Plasma was separated after centrifugation at 2000 rpm for 3 minutes, and stored in a refrigerator at -20°C. AL-9000 automatic coagulation analyzer was used for detection. Signed informed consent was obtained from all parents.

#### Statistical analysis

All data were processed by SPSS17.0 software, and normality of the data was tested. The

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**Table 3.** The results of fibrinogen and antithrombin III activity of premature infants in pregnancy-induced hypertension group and absent pregnancy-induced hypertension group ( $\bar{X} \pm SD$ )

Groups	cases	Within 24 hours after birth		The fifth day after birth	
		FIB (g/L)	AT-III (%)	FIB (g/L)	AT-III (%)
Pregnancy induced hypertension group	46	1.117±2.01	32.35±5.04	1.389±1.20	36.77±7.12
Absent pregnancy induced hypertension group	50	1.426±2.60	39.53±9.26	1.490±1.09	1.490±1.09
t		1.562	2.017	1.165	2.159
P		<0.01	<0.05	2.159	<0.05

**Table 4.** The results of fibrinogen and antithrombin III activity of premature infants in between less than 34 weeks group and 34-37 weeks group ( $\bar{X} \pm SD$ )

Groups	Cases	Within 24 hours after birth		Day 5 after birth	
		FIB (g/L)	AT-III (%)	FIB (g/L)	AT-III (%)
Less than 34 weeks group	51	1.149±3.01	30.07±8.00	1.305±1.23	35.27±7.91
34-37 weeks group	45	1.38±2.97	39.40±7.16	1.483±1.36	41.33±6.09
t		2.214	1.462	2.367	1.391
P		<0.01	<0.05	<0.01	<0.05

experimental data were expressed as mean  $\pm$  standard deviation ( $\bar{X} \pm S$ ). t-test was used according to nature of the data, and  $P < 0.05$  indicated significant difference.

### Results

As indicated by **Table 1**, among the premature infants of less than 34 weeks in gestational age, the levels of plasma fibrinogen and antithrombin III activity in maternal PIH group within 24 hours and on day 5 after birth were lower compared to maternal absent PIH group, respectively, with significant differences ( $P < 0.05$ ).

As shown by **Table 2**, among the premature infants with gestational age of 34-37 weeks, the levels of plasma fibrinogen and antithrombin III activity in maternal PIH group within 24 hours and on day 5 after birth were lower compared to maternal absent PIH group, with significant differences ( $P < 0.05$ ).

As revealed by **Table 3**, the fibrinogen and antithrombin III activity of premature infants in PIH group during the early stage after birth were lower than those in absent PIH groups, with significant differences ( $P < 0.05$ ).

As shown by **Table 4**, the fibrinogen and the antithrombin III activity of premature infants in less than 34 weeks group within 24 hours and day 5 after birth were lower than those in 34-37

weeks group, with significant differences ( $P < 0.05$ ).

Further analyses indicated that there was a positive correlation between fibrinogen and the antithrombin III activity (data not shown).

### Discussion

Previous studies have demonstrated that AT-III consumption is decreased during pregnancy due to the binding of coagulation factors of higher activity and AT-III and subsequent formation of complex [7]. AT-III level is lower in pregnancy-induced hypertension women, thereby causing high blood coagulation status [4, 8]. This study found that the AT-III activity of premature infants delivered by the mothers with PIH in the early stage after birth was lower than that in absent PIH group. It was speculated that it may be related to high coagulation status of the mother, but the mechanism remains to be further studied.

It is pointed out that neonates experience intermittent transient hypoxia during the process of birth due to the mechanical pressure from uterine contraction, so as to adapt to the new cycle after birth. During the process, there are vascular endothelial injuries, leading to activation of the coagulation and fibrinolytic system [9], which may be related to the lower level of the factors involved in coagulation-anticoagulation-

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fibrinolytic system during the early stage after birth. It is speculated that maternal PIH may lead to the activation of the coagulation and fibrinolytic system, but the mechanism is still unknown.

Various pathologic conditions of premature infants may cause disseminated intravascular coagulation (DIC), and the activity of FIB and AT-III shows consumable decline. In this study, the activity of FIB and AT-III in the premature infants was lower, but DIC was absent. Therefore, it is inferred that FIB and AT-III levels lower than normal reference values do not mean DIC.

In conclusion, FIB and AT-III levels in premature infants are lower. And the smaller the gestational age, the lower the levels. Moreover, they are related to maternal pregnancy-induced hypertension, bringing the risk of bleeding to premature infants. After birth, monitoring on dynamic changes of FIB and AT-III levels is clinically significant to prevent bleeding in premature infants, but it is limited to monitor occurrence of DIC, which remains to be further studied.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Peng Liu, Pediatric Neonatal Intensive Care Unit, Shanxi Dayi Hospital, Longcheng Street, No. 99, Taiyuan 030032, China. Tel: +86+0354-3103296; Fax: +86+0354-3103296; E-mail: liupl2015@126.com

### References

- [1] Tay SP, Cheong SK, Boo NY. Circulating tissue factor, tissue factor pathway inhibitor and D-dimer in umbilical cord blood of normal term neonates and adult plasma. *Blood Coagul Fibrinolysis* 2003; 14: 125.
- [2] Kuang WY, Wang XL and Zhu XY. Premature D-dimer and fibrinolytic enzyme dynamic change of the original research. *China's New J Pediatr* 2006; 21: 136
- [3] Zhong WP, Gao L, Cui YP, Huang B, Wan JX, Liu M and Jiang D. PT, FIB, FM, DD, PLT test on maternal diagnosis of DIC. *Pract Med J* 2005; 21: 2800.
- [4] Zou QY and Deng CQ. The laboratory tests and application of modern thrombosis and hemostasis. Beijing: People's Medical Publishing House; 2012; 2004: 25
- [5] Peng LM and Deng CQ. The laboratory tests and application of modern thrombosis and hemostasis. Beijing: People's Medical Publishing House; 2004. pp. 25.
- [6] Li JR, Liu GM and Chen SH. Pregnant women in labor D-dimer coagulation four changes and its significance in labor. *Chinese Journal of Medical Test* 2010; 11: 231-232.
- [7] Zhang YM and Jiang YQ. Pregnant women blood plasma fibrinogen and D dimer and dynamic monitoring of the AT-III clinical significance. *Journal of Clinical Inspection* 2007; 25: 229.
- [8] Wang HY. The middle of a pregnancy pregnant women blood FIB content, the AT-III and PC activity determination and significance. *Med World* 2009; 23: 501-502.
- [9] Jin HZ, Huang DM and Guan XJ. *Practical neonatology*, 3rd edition. Beijing: People's Medical Publishing House; 2003. pp. 695.