Correlation between the coagulation test and neonatal hyperbilirubinemia

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Abstract

Background

The coagulation test is used to diagnose the hematological diseases. Little is known about correlation between the coagulation test and neonatal hyperbilirubinemia. The aim of the study was to describe neonatal coagulation test in infants with neonatal hyperbilirubinemia.

Methods

Data were collected from newborns who had neonatal hyperbilirubinemia and healthy in Chengdu Second People's Hospital. Prothrombin time(PT), Thrombin time(TT), Fibrinogen(Fbg), activated partial thromboplastin time(APTT), and calculated international normalized ration(INR) values were recorded. Linear relationship between INR and level of total bilirubin and indirect bilirubin were analysed by linear regression. Comparisons of two groups were made by GraphPad Prism 8.

Results

In this case-control study, the mean PT, APTT level were significant higher in the infants with hyperbilirubinemia group compared to the healthy infants. We found the correlation between INR and total bilirubin($R = 0.3327$; $P < 0.0001$). There was also correlation between INR and indirect bilirubin($R = 0.3402$; $P < 0.0001$).

Conclusions

PT, APTT were significant high in neonatal hyperbilirubinemia group. Correlation were observed between the coagulation test and neonatal hyperbilirubinemia.

Background

Neonatal hyperbilirubinemia was a common problem in newborns[1]. Hyperbilirubinema was a major risk factor for brain damage, bilirubin-induced neurologic dysfunction[2]. It was manifested through yellowish change of skin and mucous membrane[3].

And neonatal jaundice induced blood incompatibility[4]. Some studies have shown the correlation of neonatal hyperbilirubinemia include G6PD deficiency, serum vitamin D level, ASO haemolytic disease[4–6]. Some causes of significant hyperbilirubinemia were relation with erythrocyte membrane defects, red blood cell enzyme deficiencies[7, 8]. For coagulation system, the interaction of coagulation factors has been found to go beyond their traditional effect and to affect some diseases[9, 10]. So we appreciated the correlation between hyperbilirubinemia and coagulation system.

The present study was therefore to determine the relationship between PT, PATT, Fbg, TT and hyperbilirubinemia in full term neonates.

Methods

Study desigh

This study was conducted in Chengdu, Sichuang Province, China, from October 2019 through September 2020. All newborns were born and inpatients in the newborn wards of the Chengdu Second People's Hospital. The birth weight of full term neonates were included in the study. In this case-control study, 40 eligible infants with significant hyperbilirubinemia were compared with 30 healthy infants. Additionally, written consent was obtained from all of the parents before any procedures were performed. Hyperbilirubinemia was determined by testing serum bilirubin. Increasing of the total bilirubin level more than 34umol/L was considered as hyperbilirubinemia. Venous blood samples were collected and sent for prothrombin time(PT), Thrombin time(TT), Fibrinogen(Fbg), activated partial thromboplastin time(APTT), and calculated international normalized ratio(INR).

Statistical analysis

Data was entered and analysed using GraphPad Prism 8. Mean and standard deviation were used for the analysis of the data. The unpaired test was used to compare the two groups and line regression to compare the correlation in terms of the Pearson's Correlation Coefficient. For interpretation of results, significance was adopted at $P < 0.05$.

Results

In the study, we selected 70 newborns to evaluate in two groups, including 40 neonatal hyperbilirubinemia infants in the case group and 30 healthy neonatal infants in the control group. Baseline clinical characteristics were similar in the two groups(Table 1). But there was significant difference in WBC, PLT, HGB in the two groups(Table 1). The mean WBC in hyperbilirubinemia group ($12.98 \pm 4.67 \times 10^9$/L) was significantly higher than that of the control group($6.55 \pm 1.63 \times 10^9$/L)($P < 0.0001$). The mean PLT in hyperbilirubinemia group($329.25 \pm 76.77 \times 10^9$/L) was significantly higher than that of the control group($255.13 \pm 38.11 \times 10^9$/L)($P < 0.0001$). The mean HGB in hyperbilirubinemia group(162.15 ± 17.41 g/L) was significantly higher than that of the control group(134.33 ± 11.25 g/L)($P < 0.0001$).

When Comparing the neonatal hyperbilirubinemia groups and the control groups using coagulation test, there was significant difference in PT, INR, APTT(Table 2). The mean PT in hyperbilirubinemia group(12.54 ± 1.39 second) was significantly higher than that of the control group(11.3 ± 0.63 second)($P < 0.0001$). The mean INR in hyperbilirubinemia group(1.14 ± 0.13) was significantly higher than that of the control group(1.03 ± 0.06)($P = 0.0001$). The mean APTT in hyperbilirubinemia group(47.1 ± 8.89 second) was significantly higher than that of the control group(27.67 ± 1.97 second)($P < 0.0001$).

As shown, the relationship was observed between INR and level of total bilirubine(R = 0.3327;P < 0.0001) (Fig. 1). As shown in Fig. 2, the relationship was also observed INR and level of indirect bilirubin(R = 0.3406; P < 0.0001).

Table 1
Clinical characteristics between the significant neonatal hyperbilirubinemia groups and the control groups

Characteristics	**hyperbilirubinemia groups(n = 40)**	**control groups(n = 30)**	**P**
	Mean ± SD	**Mean ± SD**	
Sex(males/females)	22/19	15/15	
Birth weight(g)			
Age(days)	4.7	6.7	
Mode of delivery			
Vaginal delivery	22	15	
Caesarean delivery	18	15	
WBC($3.5–9.2 \times 10^9$/L)	12.98 ± 4.67	6.55 ± 1.63	<0.0001
RBC($4.09–5.74 \times 10^{12}$/L)	4.68 ± 0.58	4.66 ± 0.36	0.8819
PLT($85–303 \times 10^9$/L)	329.25 ± 76.77	255.13 ± 38.11	<0.0001
HGB(131–172 g/L)	162.15 ± 17.41	134.33 ± 11.25	<0.0001

Table 2
Comparison of various characteristics between the significant neonatal hyperbilirubinemia groups and control groups

Variables	hyperbilirubinemia groups(n = 40) Mean ± SD	control groups(n = 30) Mean ± SD	P
PT(9.3–12.4 Second)	12.54 ± 1.39	11.3 ± 0.63	<0.0001
INR(0.86–1.15)	1.14 ± 0.13	1.03 ± 0.06	0.0001
Fbg(2–4 Second)	2.66 ± 0.73	2.92 ± 1.18	0.0594
APTT(22.3–32.5 Second)	47.1 ± 8.89	27.67 ± 1.97	<0.0001
TT(16-21.6 Second)	17.91 ± 1.39	17.87 ± 2.32	0.620
PCT	1.045 ± 1.21		<0.05
Hyperbilirubine			
Total(0–26 umol/L)	208.91 ± 66.28	5.9 ± 3.37	<0.0001
Direct(0–11 umol/L)	12.5 ± 4.07	1.96 ± 1.33	<0.0001
Indirect(3.4–17.1 umol/L)	199.72 ± 64.33	3.98 ± 2.31	<0.0001

Discussion

The study found the relationship between coagulation test and hyperbilirubinemia in infants. The mean PT, APTT level were significant higher in the infants with hyperbilirubinemia group compared to the healthy infants. At the same time, the mean serum PCT level was higher in the infants with hyperbilirubinemia group. In our study, the WBC, PLT and HGB level in hyperbilirubinemia group were higher than the healthy group($P < 0.0001$). We found the correlation between INR and total bilirubin($R = 0.3327$; $P < 0.0001$). There was also correlation between INR and indirect bilirubin($R = 0.3406$; $P < 0.0001$).

Hyperbilirubinemia often occurred in infants without apparent reason[11]. The causes of hyperbilirubinemia and effective prevention strategies have recommended as clinical guidelines[12]. The American Academic of Pediatrics(APP) recommends a follow-up visit after 48–72 h of the newborns discharged[13]. For the main cause of neonatal hyperbilirubinemia, a large of study have received developments[14]. Compared with other study, we used INR to evaluate the correlation between hyperbilirubinemia and coagulation. The coagulation system have easily activated by inflammation, severe disease in human[15]. Therefore, in this study, we evaluated the hyperbilirubinemia and health groups, PT and APTT were significantly prolonged in infants with hyperbilirubinemia than health control and there was significant difference($P < 0.0001$).

Conclusion

In summary, our study suggested that hyperbilirubinemia in infants may induce coagulation system to change. Maybe, the change of coagulation system may be a cause of early significant hyperbilirubinemia. Moreover, it appears to have a pathogenic potential in newborns, high PLT may be a potential problem. Importantly, we may consider coagulation system when hyperbilirubinemia was observed.

Abbreviations

PT: Prothrombin time, TT: Thrombin time, Fbg: Fibrinogen, APTT: activated partial thromboplastin time, INR: international normalized ration, WBC: White blood cell, RBC: Red blood cell, PLT: Platelet, HGB: Hemoglobin, APP: The American Academic of Pediatrics

Declarations

Competing Interests

The authors have no conflicts of interest to declare.

Ethical approval and consent to participate

The study was approved by the Ethics Committee of Chengdu second people's hospital, China and conducted according to the principles in the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and /or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Zhou Fangye contributed to the original design, the data analysis and writing of the manuscript. Li Lei contributed to the data collection. Fu Rong contributed to the editing the manuscript.

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Figures

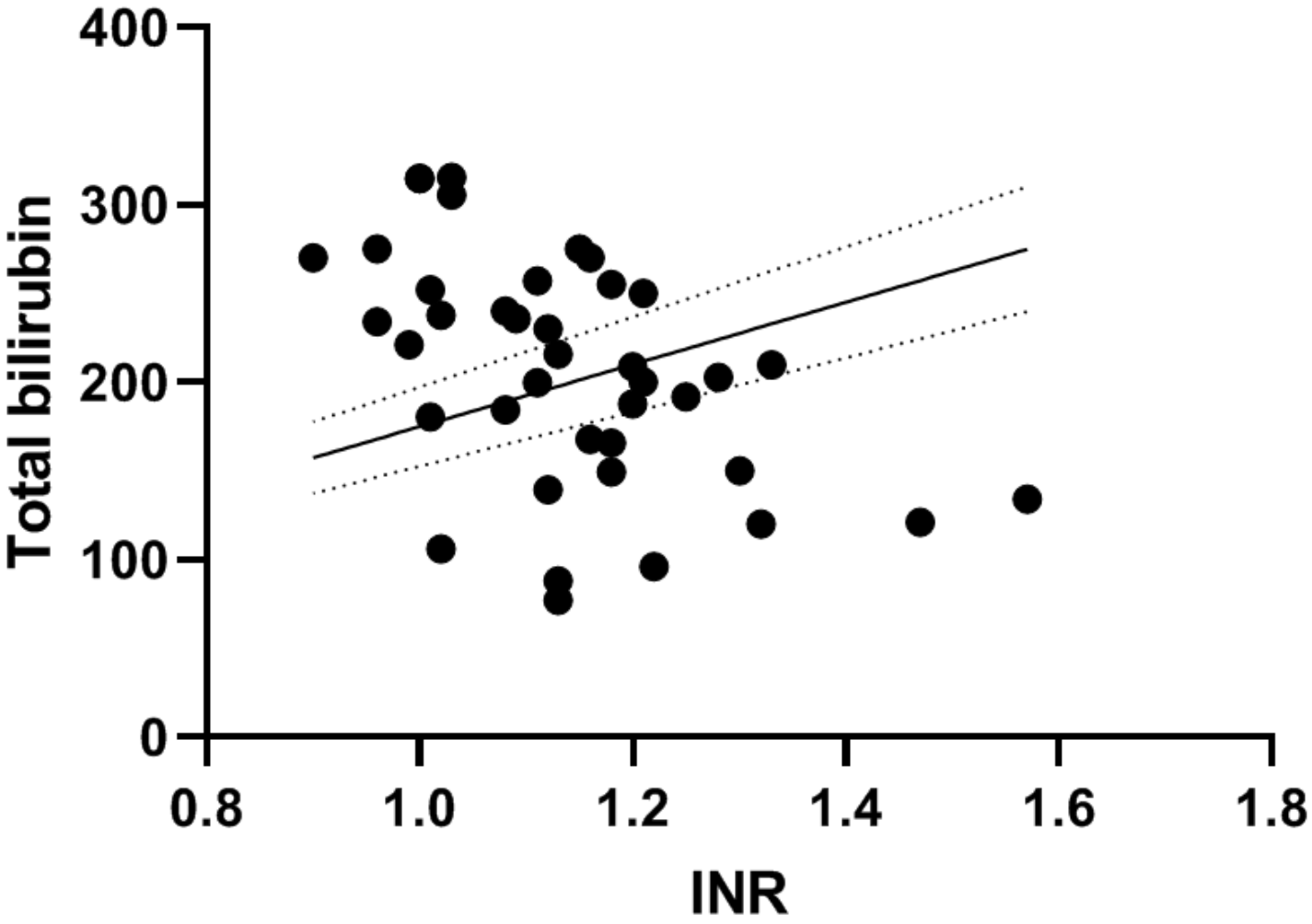

Figure 1

Linear relationship between INR and level of total bilirubin(R=0.3327; P<0.0001)

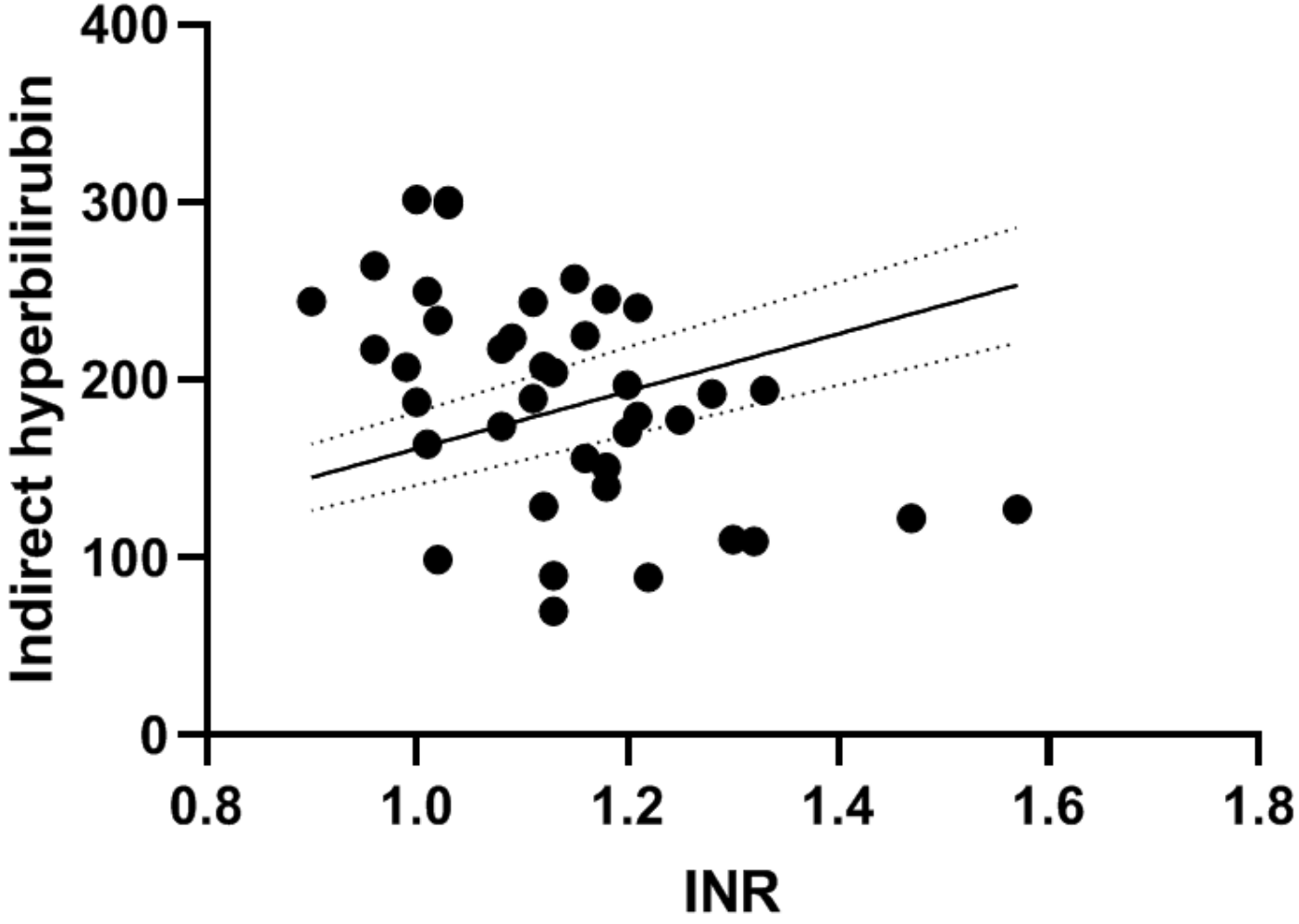

Figure 2

Linear relationship between INR and level of indirect bilirubin(R=0.3406; P<0.0001)