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Correlation between Alkaline Phosphatase and Neonatal Jaundice

Maryam Saboute[1], Aco Mahmoudian[2], Nasrin Khalesi[2]*, Zahra Vahedi[3], Nastaran Khosravi[2], Leila Allahqoli[4]

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Abstract

Background: Hyperbilirubinemia is one of the most common neonatal disorders and one of the risk factors of neurological complications. So this study was conducted to evaluate the correlation between alkaline phosphatase (ALP) and pathological jaundice.

Methods: A case-control was performed on term neonates with and without pathological jaundice who were referred to the Hazrat-e-Ali Asghar Hospital in 2017. In both groups, cases (neonates with pathological jaundice, n=153) and control (neonates with and without pathological jaundice, n=153) levels of alkaline-phosphatase and serum total bilirubin were evaluated with biochemical tests. Moreover, other data were also recorded from their history and clinical examinations. In addition, the severity of jaundice, duration of hospitalization, type of required treatment, and probable complications after the treatment were considered in follow-up. Data were collected by checklist and entered to SPSS v.20. ALP level and its relationship with serum total bilirubin compared between two groups.

Results: Mean level of ALP was 411.3 ± 134.2 U/L in the case group and 338 ± 131.4 U/L in the control group. Serum total bilirubin level was 11.9 mg/dl in the case group and 6.2 mg/dl in the control group. ALP levels in the case group were significantly more than the control group (p=0.001). There was no correlation between ALP and serum total bilirubin level in neonates in the case group (p=0.532). There was no statistically significant relationship between alkaline phosphatase level and gender of neonates, but the relationship of ALP level with types of delivery was statistically significant (p=0.002). There was not a significant relationship between ALP level with hospitalization duration (p=0.371).

Conclusion: The result of this study showed that there is no correlation between ALP levels and pathological jaundice in patients, although this issue needs to be approved by the other studies.

Keywords: Pathological Jaundice, Alkaline Phosphatase, Serum Total Bilirubin Level, Neonate

Conflicts of Interest: None declared
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Introduction

Hyperbilirubinemia is the most prevalent cause of hospitalization in term and premature neonates. Hyperbilirubinemia is seen in about 60% of term and 80% of preterm neonates (1). Inability to recognize and treat pathological hyperbilirubinemia may lead to Kernicterus with its possible neurodevelopmental disability, so an assessment of the risk of development of hyperbilirubinemia and prompt treatment is crucial (2, 3). Several methods have been used to determine the risk of pathological jaundice (3). Recently ALP level after birth has been introduced as a marker for determining hemolysis and pathological jaundice (2).

ALP is a group of isoenzymes which located on the outer layer of the cell membrane like hepatocytes; they hydrolyze the organic phosphate acids in the extracellular space (4). This enzyme has two forms which are tissue-specific and tissue nonspecific. Tissue-specific forms found in the intestine, placenta, and germinal tissue are

Corresponding author: Dr Nasrin Khalesi, khalesi.n@iums.ac.ir

1. Department of Neonatology, Akbar Abadi Hospital, Iran University of Medical Sciences, Tehran, Iran
2. Department of Neonatology, Ali Asghar Hospital, Iran University of Medical Sciences, Tehran, Iran
3. Pediatric Department, Firooz Abadi Hospital, Iran University of Medical Sciences, Tehran, Iran
4. Iran University of Medical Sciences, Tehran, Iran

↑What is "already known" in this topic:
Recently, few studies have suggested that alkaline phosphatase (ALP) can be used in predicting neonatal jaundice.

→What this article adds:
The level of ALP in the case group was higher than the control group, but there was no correlation between ALP and serum total bilirubin level in neonates in the case group.

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tissue-specific, where they are expressed in physiological conditions but may contribute to the circulating pool of serum ALP under specific situations when there is increased stimulation of their production. The tissue-nonspecific one is most of the circulating form in serum. It is produced out of a single gene in the liver, bone, and kidneys. This form has a similar amino acid sequence but they have different carbohydrate and lipid side chains; so after post-translational changes have their unique physicochemical properties (5, 6). The half-life of this ALP is 7 days, and clearance from the serum is independent of the bile duct capacity or liver function capacity. Although the site of degradation of alkaline phosphatase is not known, the liver is a source of it in most patients with elevated enzyme levels (7). Since there is no strong evidence that ALP can be a predictor of pathological hyperbilirubinemia, so this study was conducted to evaluate the correlation between alkaline phosphatase (ALP) and pathological jaundice.

Methods

This case-control study was performed on term neonates who were referred to the Hazrat-e-Ali Asghar Hospital in 2017. Neonates were divided into two groups with and without pathological jaundice. Neonates with pathological jaundice were considered as a case group and neonates without pathological jaundice as a control group. Based on the data reported by Ahmadpour-Kacho and co-workers, and the incidence of hyperbilirubinemia and the diagnostic sensitivity of ALP was 9.8% and 80%, respectively (3), a minimum sample size of 150 was determined for each group, with an alpha error of 0.05 and a study power of 90%.

All term neonates with and without pathological jaundice who were fulfilled the following inclusion criteria were enrolled in the study with convenience sampling: 1) term pregnancy, 2) with healthy mother, 3) any mode of delivery, 4) no history of underlying disease. Neonates with any congenital anomaly, sepsis, any complication that aggravates hyperbilirubinemia (respiratory distress syndrome, intrauterine growth retardation (IUGR) ,or cholestatic jaundice were also excluded from this study. Neonates in the case group were those who developed pathological jaundice and needed to hospitalize for treatment. While neonates in the control group were those who were born at that hospital or had presented to the hospital for checkups and had not developed pathological jaundice. It should be said that neonates in the case and control groups were of the same age. After enrollment, blood samples were taken from all neonates (both groups) who fulfilled the inclusion criteria, and to avoid hemolysis were promptly sent to the hospital laboratory. ALP and serum total bilirubin levels were measured and evaluated with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) reference. General parameters including gender, gestational age, birth weight, mode of delivery, neonates' age extracted from their medical records. Clinical outcomes including the severity of jaundice, duration of hospitalization, type of required treatment, and probable complications after the treatment were recorded during follow-up. All data were collected in the checklist.

Statistical analysis

The data was computerized and analyzed using the Statistical Package of Social Sciences (SPSS), version 22.0 (SPSS Inc., Chicago, IL., USA). Qualitative variables were described by frequency (percentage) and compared between groups with the Chi-square test. Quantitative variables were reported by mean ± standard deviations and the one-sample Kolmogorov-Smirnov test was used to test the normal distribution of quantitative data. All data followed the normal distribution pattern. The t-test was used to compare the quantitative variables. Correlation between quantitative variables was investigated using Pearson correlation and Spearman rank correlation tests. $P < 0.05$ was considered significant.

Results

In this study, 306 neonates participated who were divided equally into two groups of case and control groups. In the case group, 51% were male and 49% were female and gender did not differ significantly between groups. Comparison of general parameters in the two groups of case

Table 1. Comparison of general parameters in the two groups of case and control groups

Variable	Case (n= 153)	Control (n= 153)	P value
Gender, n (%)			0.057*
Male	78 (51)	101 (66)	
Female	75 (49)	52 (34)	
Gestational age, W Mean± SD	38 ± 0.96		0.022**
Birth weight, gr Mean± SD	2945 (122.8)	3213 (134)	0.001**
Mode of delivery, n (%)			0.131*
Cesarean	103 (67.3)	115 (75.2)	
NVD	50 (32.7)	38 (24.8)	

Abbreviations: N: number, W: week, SD: Standard deviation, gr: gram
* Chi-square test
**Student's t test

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Table 2. Comparison of mothers and neonates' blood group in two groups

Blood group	Mother		Neonate
	Case (n = 153)	Control (n =153)	Case (153)
	N (%)		
AB^+	9 (6.7)	14 (9.4)	6 (4.1)
AB^-	3 (2.2)	4 (2.7)	-
O^+	64 (47.4)	41 (27.5)	45 (30.5)
O^-	6 (3.9)	4 (2.7)	9 (6.1)
A^+	24 (15.7)	48 (32.2)	48 (32.7)
A^-	3 (2.2)	9 (5.9)	6 (4.1)
B^+	14 (10.4)	29 (19.5)	27 (18.4)
B^-	12 (8.9)	-	6 (4.1)
Total	135	149	147

Table 3. Comparison of the level alkaline phosphatase and serum bilirubin in two groups

Variable	Group	Mean	Standard deviation	p value*
Alkaline phosphatase	Case	411.3	134.2	0.001
	Control	338	131.4	
Bilirubin	Case	11.9	3.15	0.001
	Control	6.2	1.43	

Student's t test

and control groups are presented in Table 1.

The most frequent blood group among mothers of the case group was O^+ (47.4%) and the control group was A^+ (32.2%). This frequency in case group of neonates was A^+ (32.7%). The blood groups of the control neonates were not recorded (Table 2).

The mean level of ALP in male and female was 336.8±138.2 and 340.1±127.4, respectively. The results revealed that there was no significant difference in the level of ALP between male and female patients (p=0.860). ALP level in neonates in the case group was statistically significantly higher than the control group (p=0.001). Comparison of the level alkaline phosphatase and serum bilirubin in two groups are summarized in Table 3.

In addition, our results showed that there was no correlation between the level of ALP and serum bilirubin in the case group (p = 0.532) (Pearson correlation coefficient =0.052) (Fig. 1). In the neonates of the case group, the mean hospitalization day was 3.07±2.52, and twenty-seven were hospitalized for less than 1 day. The differences in the level of ALP were not statistically significant in neonates with less and no more than 1-day hospitalization (p=0.371).

The mean birth weight in the control group was more than in the case group. There was not any correlation between birth weight and level of ALP in the case group (p=0.688) (Pearson correlation coefficient =- 0.33) (Fig. 2).

Discussion

Pathological jaundice has lots of harmful effects on neonates if it doesn't diagnose quickly. (8, 9), recently ALP level after birth has been introduced as a marker for determining hemolysis and pathological jaundice (2). So this study was conducted to evaluate the effect ALP in predicting of pathological jaundice. In the present study, the mean level of ALP was 374.65. In Ahmadpour et al. study the mean level of ALP was 325.24 ± 85.04 IU/L (3) and in Abbasian coworkers' study was 314.3±122.4 IU/L (10).

In this study, compared to control group ALP level in neonates of the case group was statistically significantly higher. The results of previously published studies have revealed that there was a significant difference in the levels of cord blood ALP between the non-jaundiced and

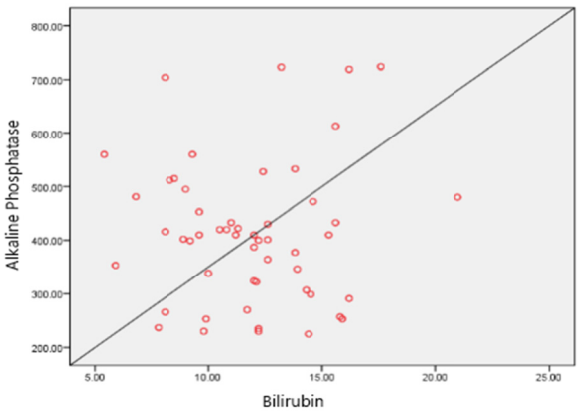

Fig. 1. Scatter plot of alkaline phosphatase level and serum bilirubin in case group

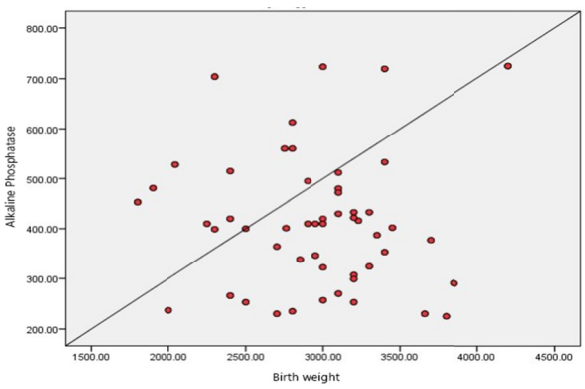

Fig. 2. Scatter plot of alkaline phosphatase level and birth weight in patient group

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clinically jaundiced newborns, and it was significantly higher in patients with hyperbilirubinemia requiring treatment (2, 3).

In the present study, although ALP level in neonates of the case group was statistically significantly higher than the control group, there was no correlation between the level of ALP and serum bilirubin case group. Inconsistent with the results of the present study, in a cross-sectional study by Nalbantoglu et al. ALP level there was significant relationship between ALP with hyperbilirubinemia (7). Ahmadpour-Kacho reported that the cord blood ALP level can be used as a predictor of neonatal jaundice (3). This issue calls for well-founded studies of appropriate design.

In this study, the results showed that the most frequent blood group among the mothers of the case and control groups was O + and A +. It was declared that the most prevalent reason for jaundice in neonates is heterogeneousity of their blood group and mothers (blood group of mother O and neonate A or B). According to Boskabadi et al. study the hemolytic etiologies of jaundice was 78%, which were ABO and RH incompatibility and G6PD deficiency (11). Therefore, the awareness of physicians, nurses, and families about the importance of ABO incompatibility evaluation should be increased. It can be effective in reducing the incidence of jaundice and start their treatment as soon as possible. Birth weight in the control group was higher than case group, but there was not a significant relationship between ALP and birth weight. To our knowledge, there were no related studies that has been addressed neonatal weight and ALP levels. Therefore, it was not possible to compare this finding with other studies.

Conclusion

ALP level in the case group was significantly more than the control group but there was no significant correlation between ALP level and serum bilirubin. This issue needs to be approved by the other studies.

Ethical approve and consent to participate

This study was approved by ethics committee of Iran University of Medical Sciences (IR.IUMS.REC. 1396.8921215.42). To ensure confidentiality, no participant was recorded by name. The results were only reported in groups.

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Conflict of Interests

The authors declare that they have no competing interests.

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