

Prognostic Factors on Low-Birth-Weight Infants of Atresia and/or Tracheoesophageal Fistula: a Cohort Study

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Research

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Abstract

Background: Low-birth-weight is the main factor affecting the survival rate of esophageal atresia (EA)/tracheoesophageal fistula (TEF). The study aims to summarize the factors influencing the prognosis of EA/TEF, which is expected to be helpful for clinical diagnosis and treatment.

Methods: A retrospective data analysis was performed in our hospital underwent TEF/EA repair between January 2012 and January 2015. The incidence of preoperative, intraoperative critical events and postoperative complications and overall survival (OS) were compared between two groups of infants: 81 patients with EA/TEF, 24 low-birth-weight patients (<2500 g) with EA/TEF and 57 patients (>2500 g). The morbidity was compared between patients with stress hyperglycemia and euglycemia postoperatively.

Results: The overall incidence of preoperative, intraoperative critical events and postoperative complications in low-birth-weight patients was significantly higher ($P=0.002$, $P=0.001$, $P=0.001$), but OS was lower (75.9% vs 92.3%, $p=0.027$). OS of patients with stress hyperglycemia postoperatively was lower than that of euglycemia (81.0% vs 93.6%, $p=0.03$).

Conclusions: Low-birth-weight still was the main factor that impacted on the prognosis of EA/TEF. The lower the birth weight was, the higher the mortality was. Postoperative stress hyperglycemia was one of the important factors that influenced survival rate.

Background

Esophageal atresia with or without tracheoesophageal fistula is a severe neonatal malformations [1–3]. With the improvement of neonatal surgical techniques and perioperative nursing care, the overall survival(OS) rate nearly reached more than 90%, which includes the very-low-birth-weight newborns with or without cardiac abnormalities. However, newborns with severe deformity still suffered higher mortality [4]. In China, some large clinical centers have reported the overall survival rate of EA /TEF is about 85%-91.4%, but most of them are full-term infants and without heart malformation [5–7]. In recent years, some retrospective studies have shown that low birth weight and concomitant heart disease still cause a most important impact on the survival rate of newborn [8–10].

However, there are few systematic studies and rigorous follow-ups. Our study mainly summarized and analyzed the prognostic factors of low-birth-weight children with esophageal atresia in our hospital in the past seven years, so as to guide clinical treatment and prognosis judgment, and further improve the survival rate of esophageal atresia in China.

Patients And Methods

Patients

From January 2012 to January 2015, 81 cases of congenital esophageal atresia were admitted to our hospital. There were 47 male and 34 female patients in our study, which included 2 cases of type I (2%), 1 case of type II, 8 cases of type IIIA (10%), 69 cases of type B, 1 case of type C and 0 case of type D. The average birth weight of all the children was 2.68 ± 0.54 kg (1.4 ~ 4.0 kg), among which 24 cases had the birth weight of less than 2500g, accounting for 29.6%. The average gestational age was 38.4 ± 2.27 weeks, and 8 cases were preterm infants (less than 37 weeks). Twenty-three children were associated with congenital malformations (1 with neurological malformation, 2 with genitourinary malformation, 4 with skeletal and extremities malformation, 3 with gastrointestinal malformation, 2 with chromosomal abnormalities of trisomy 21 and trisomy 18), and 11 with concomitant syndromes (VATER/VACTERL or CHARGE). All the patients were evaluated by echocardiography before operation and 21 cases were diagnosed with various cardiac malformations (table 1). Among all the patients undergoing surgery, 4 were long-segment type, among which 3 were children with low birth weight. Among the 81 common types, 21 were children with low birth weight, accounting for 25.9%.

Surgical procedure

All the patients were performed by the operation through the 5th right intercostal approach into the chest. 4 cases of long-segment esophageal atresia were treated with delayed one-stage anastomosis, and the remaining 77 cases were treated with one-stage operation.

Observational analysis index

1. Retrospective analysis was performed to compare the survival rates of infants with low birth weight and those with non-low birth weight with esophageal atresia, and the correlation between survival rates and birth weight was analyzed.
2. Normal birth weight and low birth weight of preoperative acute events (including high fever, respiratory failure, difficult to control blood flow dynamic changes in drug control, etc.) and intraoperative acute events (including intubation, ventilation, difficulties, blood oxygen saturation < 90%, systolic blood pressure in 60 MMHG or higher than 140 MMHG, incidence of intraoperative blood transfusion, etc.) were compared.
3. Postoperative complications of low birth weight (esophageal stenosis, esophageal anastomotic fistula, pleural effusion, right upper lung atelectasis, pneumothorax, tracheal softening, etc.) were recorded. Postoperative mechanical ventilation duration, ICU monitoring time, thoracic drainage time and hospitalization time were analyzed and compared between low-birth-weight and normal-birth-weight infants.
4. The relationship between the postoperative stress hyperglycemia (plasma glucose, glucose oxidase method) and birth weigh were investigated, and the correlation between stress hyperglycemia and postoperative complications were also evaluated.
5. Independent factors affecting survival rate (such as low birth weight, cardiac malformation and postoperative hyperglycemia, etc) were analyzed.

Statistical analysis

SPSS19.0 was used for data analysis. Mann-whitney u-test and t-test were used for comparison between groups. The classified data was analyzed by the chi-square test. Survival rate as two classification variables was put into a dependent variable, low birth weight (< 2.5 kg), stress hyperglycemia (> 8.0 tendency/L), cardiac malformation (removal of patent foramen ovale and patent ductus arteriosus) into the covariate. In order to remove influence from each other, we used the method of gradually eliminating backward modeling to establish a logistic regression model and analyze its influencing factors.

Results

The effect of birth weight on survival

There were 81 cases of esophageal atresia and 24 cases of birth weight <2500g (30.9%), including 6 cases of very low birth weight <2000 g and 2 cases of extremely low birth weight <1500g (figure 1). In our study, 57 patients were born with normal birth weight. 5 died after surgery and the OS was 91.2%. OS was 75.9% in low-birth-weight infants, with statistical difference between the two groups (P=0.027). To analyze the data associated birth weight with survival rate, we found birth weight is positive correlation with survival rate (Pearson correlation coefficient of 0.936, P = 0.014, Fig 2). That is, the lower the birth weight, the lower the survival rate.

Among the 7 postoperative deaths of low-birth-weight infants, 1 case was long-segment esophageal atresia, which resulted in uncontrollable postoperative infection and pneumonia, and soon multi-system organ failure. The other 6 cases were accompanied by multiple deformities, and their parents chose to give up at last.

Preoperative and intraoperative acute events

2 cases of preoperative blood oxygen saturation were lower than 90%. There were 35 cases of inhalation pneumonia, 5 of which suffered dyspnea and received endotracheal intubation. The preoperative incidence of acute events in low-birth-weight infants was 66.7% (16/24), and the incidence of acute events in non-low-birth-weight infants was 31.5% (18/57), with statistical difference (P=0.003, table 2). The incidence of preoperative acute events was higher in patients with esophageal atresia and low birth weight. The incidence of intraoperative acute events in patients with low-birth-weight was also higher than that of infants without low-birth-weight (70% vs 26%, P=0.001). The incidence of intraoperative acute events was significantly higher in patients with cardiac malformation (14 cases) than that without cardiac malformation (p=0.001). There was no significant difference in the incidence of preoperative acute events between preterm infants and full-term infants (p=0.06), but the incidence of intraoperative acute events significantly increased in preterm infants (p=0.003).

Postoperative complications in low birth-weight infants

A total of 51 postoperative complications occurred in 81 children (table 2), including 17 postoperative complications in 24 cases of low-birth-weight infants and 34 complications in 57 cases of non-low-birth-weight infants. The postoperative complications in the low-birth-weight infants were significantly higher than that in non-low-birth-weight infants ($P=0.029$). There were 13 patients suffering postoperative anastomotic fistula and the incidence of anastomotic fistula with low birth weight was higher than non-low-birth-weight infants ($p=0.03$). Pleural effusion occurred in 5 cases, pneumothorax in 5 cases, and atelectasis in 3 cases. Among the 12 cases of postoperative esophageal stenosis, 10 cases needed esophageal dilatation, and the maximum number of one case was 5 times of esophageal dilatation. Compared with normal-birth-weight infants, the duration of postoperative mechanical ventilation in low-birth-weight infants was 8.5 ± 2.9 days, and that in non-low-birth-weight infants was 3.5 ± 2.5 days, which was significantly prolonged ($P=0.001$). The duration of ICU monitoring was also prolonged (14.2 ± 5.2 days vs. 5.9 ± 6.1 days, $P=0.034$), while the thoracic drainage time and hospitalization time were not statistically significant (9.4 ± 3.1 days vs. 10.1 ± 2.2 days, $P=0.596$; 28 ± 8.5 days vs. 22.5 ± 9.1 days, $P=0.274$, figure 3).

Postoperative stress hyperglycemia

Postoperative stress hyperglycemia in our study refers to the blood glucose concentration (plasma blood glucose, glucose oxidase method) was measured two hours after the postoperative sugar-free rehydration, and the blood glucose concentration higher than 8.0mmol/L is considered to be stress hyperglycemia. A total of 37/81 children with stress hyperglycemia occurred postoperatively, including 13 children with low birth weight (13/24, 54.1%). Postoperative incidence of anastomotic fistula in children with stress hyperglycemia was significantly higher than that in children with normal postoperative blood glucose ($P=0.015$), which showed postoperative stress hyperglycemia will cause postoperative complications increased. We tested the correlation between postoperative blood glucose level and survival rate, and found a negative correlation (Pearson correlation coefficient -0.931 , $P=0.022$, figure 4).

Following-up

There were ten patients who died after discharge and 27 patients suffered gastroesophageal reflux, which were treated conservatively. 19 children still needed esophageal dilatation after discharge, and 2 children were lower in height and weight than children at the same age. Logistic regression analysis showed that cardiac malformation was the first factor to be removed ($P=0.236$), while birth weight ($P=0.012$) and postoperative stress hyperglycemia ($P=0.048$) were independent prognostic factors.

Discussion

In the treatment of congenital esophageal atresia, the effect of low-birth-weight on survival rate is still one of the important factors [8–10]. At present, Waterston's (1962) classification and Spitz's (1994) classification are well known [11]. Spitz's study identified severe congenital heart malformations as a major prognostic factor, and his rating differed from Waterston's by a birth weight of 1,500 grams. Thus, low birth weight, pneumonia, and concomitant malformation are always the three factors affecting the

prognosis of children [12]. This study shows that a series of problems caused by pneumonia, such as shock and respiratory failure, need considerable attention preoperatively and intraoperatively, but the occurrence of pneumonia is mostly caused by surgical reasons such as esophageal atresia/esophagotracheal fistula, which has been significantly improved by surgical technology. In recent years, with the improvement of NICU, and the application of carbapenem and other antibiotics, the preoperative pneumonia symptoms were well controlled, which makes the status of pneumonia among the three prognostic factors decline. Our study mainly summarized and analyzed the prognostic factors of children with low birth weight esophageal atresia. The results showed that the survival rate of children with low-birth-weight was significantly lower than that of children with normal birth weight. Some studies believe that the survival rate data of low birth weight esophageal atresis has been significantly improved compared with the previous data, and it is considered that birth-weight is not the main influencing factor [13, 14]. With the establishment of NICU in children's specialized hospitals in China and the improvement of the treatment level for various complications of low birth weight, especially the improvement of monitoring, anesthesia and nursing, the cure rate of patients with low birth weight esophageal atresia is gradually improving, but the overall survival rate is still significantly lower than that abroad [9, 12].

In our study, there were significant differences in the incidence of preoperative and intraoperative acute events between infants with low-birth-weight and those with normal-birth-weight. The results indicated patients with low-birth-weight face more risks and the accompanying heart malformations were relatively common [15]. In the analysis of this study, it was found that the impact of cardiac malformation on the survival rate was related to the type of cardiac malformation, and severe cardiac malformation such as tetralogy of fallot had a greater impact on the survival rate of patients. The mortality of esophageal atresia has significantly declined, but the postoperative complications are still high [16, 17]. In particular, anastomotic fistula and postoperative esophageal stenosis result in significantly prolonged duration of postoperative mechanical ventilation and ICU monitoring, which has a great impact on survival rate and prognosis of patients.

In our research, the effect of stress hyperglycemia on neonates may not only be a transient factor, but also interact with insulin resistance and play an important role in the prognosis of patients. Logistic regression analysis data showed that stress hyperglycemia had an independent effect on the prognosis of children with esophageal atresia. Nearly half of low-weight children (55.17%) suffered postoperative stress hyperglycemia, and the incidence of anastomotic fistula and esophageal stenosis was significantly increased in these children. The function of blood glucose regulation in children with low birth weight is unstable. Although the mechanism of damage caused by hyperglycemia to neonates is unknown, whether to give intervention is still controversial. Strict control of blood sugar with intensive insulin therapy (IIT) resulted in a 90-day increase in mortality despite a 28-day reduction in mortality [18–20]. Therefore, further studies are still needed for neonatal patients, and the benefits and risks of blood glucose control are coexisted.

Conclusions

Low-birth-weight was the main factor affecting the survival rate of esophageal atresia. Intraoperative and postoperative complications were higher. Postoperative stress hyperglycemia of low-birth-weight infants is an important factor affecting postoperative complications and survival rate, and whether and how to intervene is still worthy of further study.

Abbreviations

EA

esophageal atresia;TEF tracheoesophageal fistula OS overall survival NICU Neonatal Intensive Care Unit; IIT: intensive insulin therapy

Declarations

Acknowledgements

None.

Authors' contributions

Xiaonan Xu contributed to the conception and design of the study; Ni Zhang and Binder Li contributed to the acquisition of data and performed the experiments; Xiaonan Xu wrote the manuscript; All authors contributed to the analysis of data.

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Availability of data and materials

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

Ethics approval and consent to participate

This research was approved by the Ethics Committee of Second Hospital of Lanzhou University. All methods were carried out in accordance with relevant guidelines and regulations. Written Informed consent was obtained from all the study subjects' parents before enrollment.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

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Tables

Table 1. EA/TEF accompanied by various cardiac malformations

Cardiac malformations	n
Ventricular septal defect (VSD)	4
Atrial septal defect (ASD)	4
VSD with ASD	3
Tetralogy of fallot	2
Left heart hypoplastic syndrome	1
Double superior vena cava	1

Table 2. Comparison of preoperative, intraoperative acute events and postoperative complications between low birthweight infants and non-low birthweight infants

	low-birth-weight infants n= 24	Non-low-birth-weight infants n=57	P value
Acute preoperative events			0.02
SpO2 <90%	3	0	
Uncontrollable high fever	6	3	
mechanical ventilation	8	3	
Acute intraoperative events			0.03
Difficult intubation	9	7	
Ventilation difficult	6	4	
SpO2 <90%	3	1	
Hypotension	5	3	
hypertension	3	5	
arrhythmia	5	2	
blood transfusion	6	5	
Operating room extubation	2	12	
postoperative complications			0.027
anastomotic fistula	8	5	
Minor leak	5	4	
Serious leak	3	1	
stenosis	8	4	
pleural effusion	3	2	
pneumothorax	3	2	
pulmonary atelectasis	2	1	

Figures

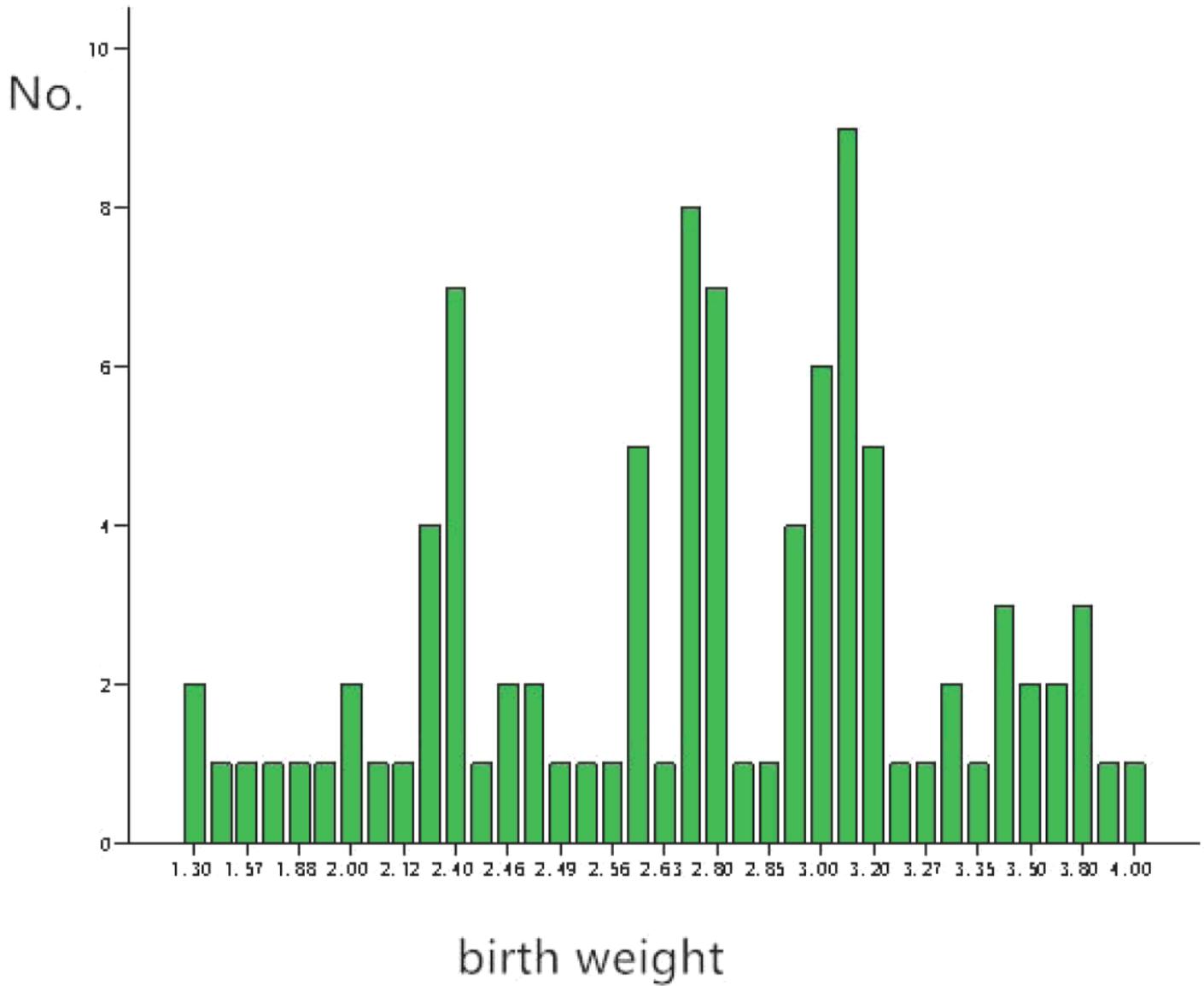


Figure 1

Birth weight distribution in all children.

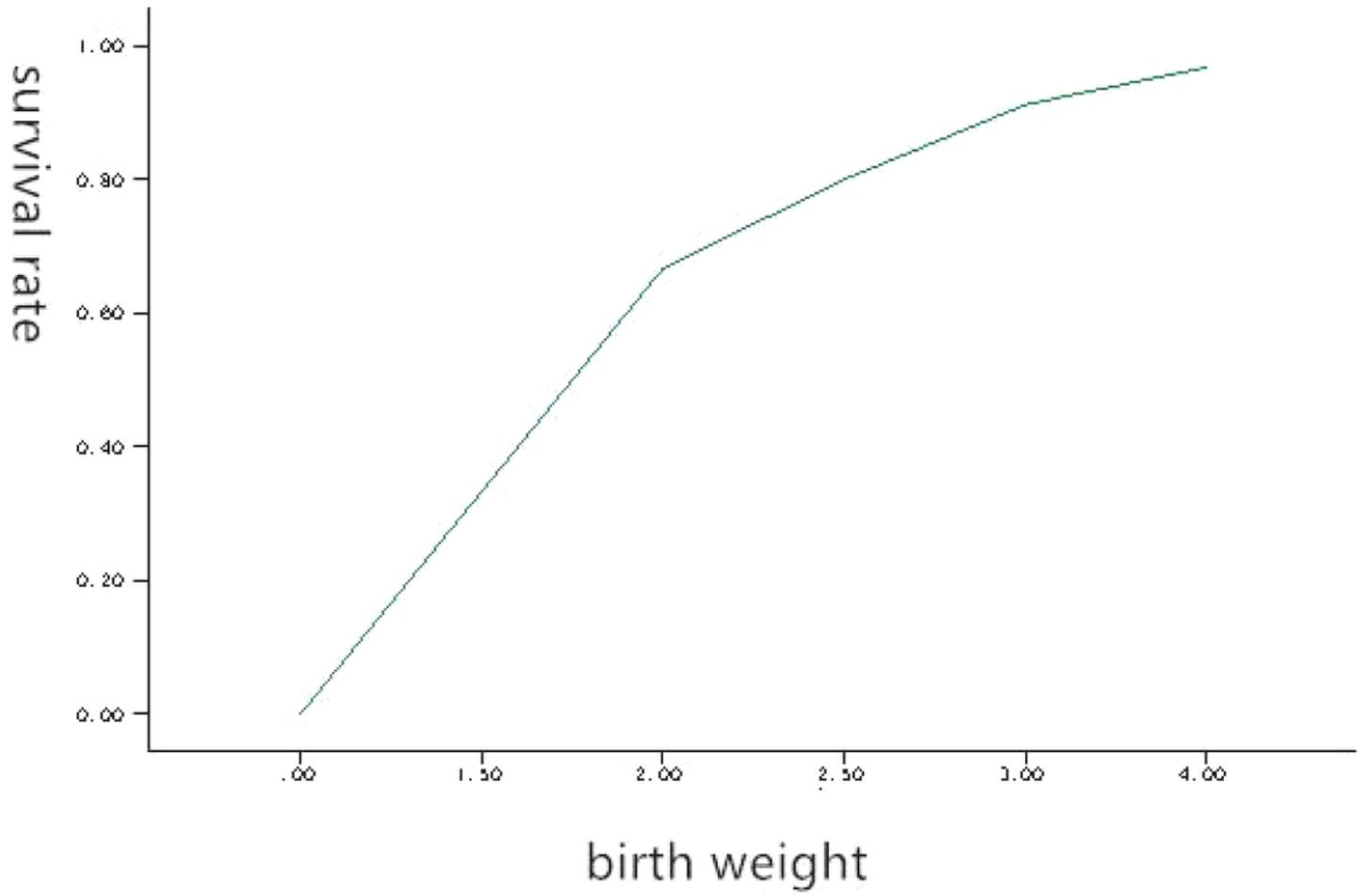


Figure 2

Birth weight was positively correlated with survival rate.

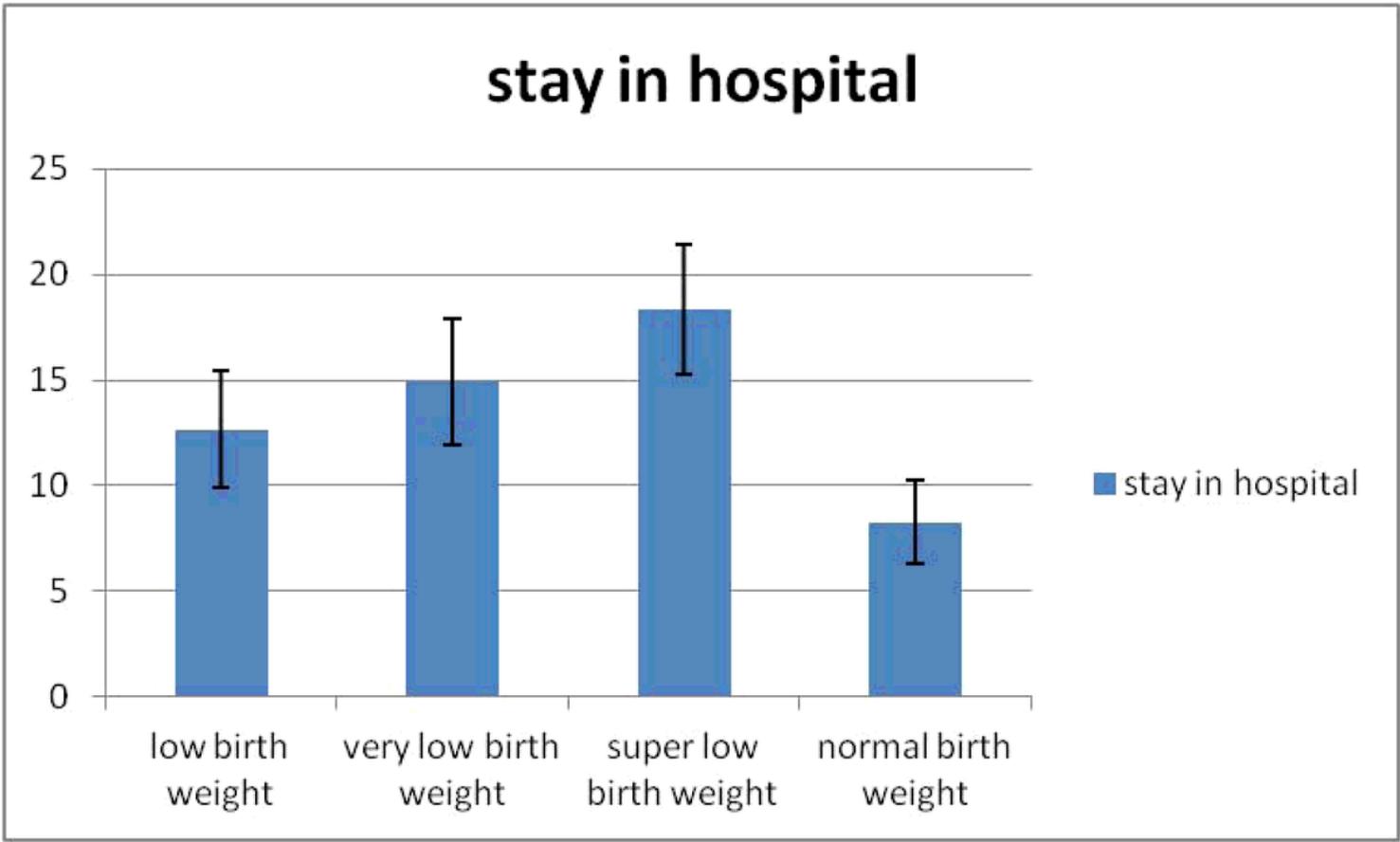


Figure 3

Days stay in hospital between different birth-weight groups.



Figure 4

Blood Glucose was negatively correlated with survival rate.