The Relationships between Sepsis and Glucosuria in Prematur Infants at H.Adam Malik Central General Hospital Medan in 2018

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ABSTRACT

Bacground : Nenonatal sepsis is a clinical syndrome of systemic abnormalities in which bactreremia occurs in the first month of life. In prematur infants the risk of hyperglycemia increases in sepsis, so glucose monitoring in the blood is needed, but it causes discomfort to the infants, so glucose monitoring in urine is non-invasive and is expected to be a marker of early sepsis.

Objective : To determine the relationship between sepsis and glucosuria at H.Adam Malik Central General Hospital Medan.

Material and Methods : A cross-sectional study of preterm infants with suspected sepsis at H. Adam Malik General Hospital Medan in December 2018-February 2019. Infants who fulfilled the inclusion and exclusion criteria were examined glucose in urine using urine dipstick and blood culture tests.

Result : In a total of 50 preterm infants, positive blood cultures were found in 13 infants (26%) with glucosuria found in 7 infants (53.8%). There is no meaningful relationship between sepsis and glucosuria. Risk factors for preterm infants experiencing glucosuria were hyperglycemia with OR 18.6; 95% CI 2.204-158.07, p = 0.001.

Conclusion : There was no significant relationship between sepsis and glucosuria

Keywords: Sepsis, glucosuria, premature infant

1. Introduction

Neonatal sepsis is still a major cause of mortality and morbidity of newborns. The incidence of sepsis in developing countries is still quite high (1.8 to 18% per 1000 births) compared to developed countries (1.5% per 1000 births). The incidence of neonatal sepsis in infants treated at the Haji Adam Malik Hospital in Medan in 2015 was 24.6%.[1,2,3,4]

Impaired glucose homeostasis often occurs especially in premature infants. Hyperglycemia often occurs 25 to 80% in premature newborns, depending on gestational age and birth weight. Inadequate liver function and lack of sensitivity of the pancreas in secreting insulin, so the risk of hyperglycemia increases in stressful episodes,such as sepsis. When glucose levels exceed the renal threshold,this glycemic instability can cause glucosuria especially in premature infants. [5,6,7,8,9,10]

Although it is well known that hyperglycemia is an early sign of sepsis, monitoring glucose levels requires repeated sampling and will cause discomfort, through urine dipstick which is a diagnostic instrument in knowing pathology in urine can be used to measure glucose levels in urine, non-invasive and is expected to be as early marker of sepsis.

2. Methods

Study Design

A cross-sectional study of preterm infants with suspected sepsis at H. Adam Malik General Hospital Medan in December 2018-February 2019. The inclusion criteria were Premature infants with gestational age <37 weeks with Symptoms and clinical signs of sepsis. The exclusion criteria were Mothers with Diabetes Mellitus and Infants with acute kidney failure caused by sepsis.

All prematur infant who fulfilled in the inclusion criteria were enrolled in this study. Informed concent was approved by parents. Urine sample collection is carried out using a JMS pediatric urine collector, by attaching the area around the genitalia, accommodating until the urine was collected. The examination was carried out with a urine dipstick. Dip the test strip in the urine (all test pads must be fully covered in urine) then remove as soon as possible. The test strip is held close to the color block, after 30 seconds compare the reaction color in the test area to the color scale on the label, see the color change from green to brown, then record the results, the recording form was semicualitative and patients were also drawn 1 ml of blood from the femoral vein by laboratory personnel for blood culture

Statistical Analysis

The collected data is processed and analyzed using computer software. Univariate analysis is used to describe the characteristics of the sample. Categorical data were presented in the form of frequencies and percentages. Bivariate analysis was used to determine the relationship of sepsis with glucosuria using chi square. The significance level and the confidence interval used were P <0.05 and 95%, respectively.

3. Results

This research was conducted at H. Adam Malik General Hospital Medan. It was found that 50 preterm infants suspected of having clinical sepsis with gestational age <37 weeks were included in this study. Most subjects (68%) were born at 33-37 weeks' gestation. A total of (60%) subjects in this study were male and (66%) subjects were born as cesaria. The average birth weight of a baby is 1800 grams.

Obtained (52%) subjects began to see signs of the onset of sepsis aged> 72 hours, hyperthermia (42%), apnoe (58%), tachypnoe (66%), tachycardia (46%), prolongation of capillary refill time> 2 seconds (32%), increased respiratory support (96%), skin discoloration such as pale / mottlet (82%), hyperglycemia (30%) and hypoglycemia (18%), metabolic acidosis (78%). From the results of this study found 58% of subjects with the results of urine dipstick were found glucosuria and as many as (26%) subjects with positive blood cultures.

Table 1. Demographic characteristics of subjects

Characteristics	*n*=50
Gender , *n*(%)	
Male	30 (60)
Female	20 (40)
Gestation age, *n*(%)	
≤ 28 week	7 (14)
28-32 week	9 (18)
33-37 week	34 (68)
The way of birth,*n* (%)	
Spontaneous parturity	17 (34)
Sectio cesaria	33 (66)
Average birth weight, gram (SD)	1800 (467.84)
Age of onset symptoms and signs of sepsis, n(%)	
≤ 72 hours	24 (48)
> 72 hours	26 (52)
Symptoms of respiratory disorders, *n*(%)	
Apnoe	29 (58)
Tachypnoe	33 (66)
Cyanosis	10 (20)
Increased respiratory support	48 (96)
Letargy ,*n*(%)	5 (10)
Symptoms of circulatory disorders,*n*(%)	
Tachycardia	23 (46)
Discoloration of the skin (pale/mottlet)	41 (82)
Hypotensi	6 (12)
Capillary refill time > 2 second	16 (32)
General symptoms, *n*(%)	
Hypertermi	21 (42)
Hypotermi	10 (20)
Symptoms of metabolic disorders, *n*(%)	
Metabolic acidosis	39 (78)
Hyperglicemia	15 (30)

Table 2. Relationship between symptoms and clinical signs of sepsis with glucosuria

Variable	Glucosuria		P*	Prevalence Ratio (PR)	Confidence interval (95% CI)
	Negative *n*(%)	Positive *n*(%)			
Hypotensi					
Yes	2 (33.3)	4 (66.7)	1.000	1.520	0.251-9.188
No	19 (43.2)	25 (56.8)			
Hypertermi					
Yes	12 (41.4)	17 (58.6)	1.000	1.063	0.341-3.313
No	9 (42.9)	12 (57.1)			
Apnoe					
Yes	7 (24.1)	22 (75.9)	0.007	6.286	1.812-21.8
No	14 (66.7)	7 (33.3)			
Takipnoe					
Yes	16 (48.5)	17 (51.5)	0.984	0.443	0.127-1.540
No	5 (29.4)	12 (70.6)			
Cyanosis					
Yes	3 (30)	7 (70)	0.488	1.909	0.431-8.463
No	18 (45)	22 (55)			
Tachycardia					
Yes	20 (87)	3 (13)	0.109	0.255	0.060-1.080
No	17 (63)	10 (37)			
Increased respiratory support					
Yes	20 (41.7)	28 (58.3)	1.000	1.400	0.083-23.737
No	1(50)	1 (50)			
Capillary refiil time					
≤ 2 second	12 (35.3)	22 (64.7)	0.274	0.424	0.126-1.426
> 2 second	9 (56.3)	7 (43.8)			
Letargy					
Yes	1 (20)	4 (80)	0.383	3.200	0.331-30.938
No	20 (44.4)	25 (55.6)			
Pale or Mottlet					
Yes	17 (41.5)	24 (58.5)	1.000	1.129	0.264-4.835
No	4 (44.4)	5 (55.6)			
Hyperglicemi					
Yes	1 (4.8)	14 (48.3)	0.001	18.667	2.204-158.07
No	20 (57.1)	15 (42.9)			
Metabolic Acidosis					
Yes	14 (35.9)	25 (64.1)	0.166	3.125	0.777-12.569
No	7 (63.6)	4 (36.4)			

Chi-Square Test

From the table above found a statistically significant relationship between apnoe and glucosuria (P = 0.007) with a prevalence ratio of 6.266, 95% CI; (1,812-21,800) and hyperglycemia (P = 0.001) with a prevalence ratio of 18,667 95% CI; (2,204-158.07)

Table 3. The relationship between sepsis and glucosuria

Blood cultur	Glucosuria		Total	RP (95% CI)	P
	Negative *n*(%)	Positive *n*(%)			
Negative	15 (40.5)	22 (59.5)	37	0.795(0.223-2.840)	0.979
Positive	6 (46.2)	7 (53.8)	13		

From the table above it can be seen that there is no significant relationship between sepsis and glucosuria (P = 0.979) with a prevalence ratio of 0.795 (95% CI; 0.223-2.840)

DISCUSSION

Prematurity is a high risk of death in neonates with the risk of developing sepsis more than 11 times compared to full-term babies.[11] In previous studies sepsis in premature infants was related to gestational age, birth weight, and time of occurrence of signs and symptoms of sepsis.[12] In our study infants gestational age 33-37 weeks most found 34 Infants (68%). This was supported by research conducted by Roeslani in 2013 at Cipto Mangunkusumo Hospital in Jakarta which showed that gestational age <37 weeks had a significant relationship to the incidence of neonatal sepsis.[13] The results of the study were different by Stoll in 2010 that the incidence of sepsis was 20% in infants 28 weeks 'gestation and 58% of infant 22 weeks' gestation.

Infants <37 weeks 'gestation affect the incidence of sepsis because passive transfor- mation of immunoglobulins begins at 8-12 weeks' gestation across the placenta, and enters the fetal circulation at 30-40 weeks 'gestation, so babies born at <37 weeks' gestation have immunity still immature and have a deficiency of Ig G antibodies against certain bacteria because these antibodies do not cross the placenta from mother to fetal blood until the end of pregnancy, so premature babies were more susceptible to infection or sepsis.

In our study the average neonatal birth weight was 1800 grams, this is in accordance with a study in Sudan in 2014 and a study in Ghana in 2018 Find premature babies weighing 1500-2500 grams associated with research related studies conducted in Semarang in 2008 from 41 neonatal sepsis obtained 39 infants with birth weight 2500-4000 grams this is supported by research in Manado 2013 gained birth weight of all patients with neonatal sepsis most 2500-4000.[14,15,16] According to theory, low birth weight babies (LBW) Complement system activity, monocyte-macrophages, chemotaxic activity, bactericides, and the presentation of antigens by cells in an imperfect inflammatory tissue response

Apnoe in preterm infants is an abnormal breathing pattern that is characterized by stopping breathing for more than 20 seconds, or less than 20 seconds but accompanied by bradycardia, cyanosis, or changes in muscle tone.[17] In our study subjects were found to have apnoe in 29 babies (58%) and requires 48 respiratory support (82%). In premature infants suspected sepsis symptoms of respiratory distress apnoe, takipnoe, cyanosis, and babies who survive weighing less than 1500 grams at birth experience apnoe episodes and require ventilatory and medical support and in low birth weight infants imperfect respiratory regulators, Lung surfactant is still lacking, so that its development is not perfect, respiratory muscles and ribs are still weak which results in lack of oxygenation to the brain, if oxygen is lacking then anaerobic bacteria easily develop causing easy infection.

Hyperglycemia in sepsis also originates from the process of glycolysis in the muscles and lipolysis, gluconeogenesis and liver glycolysis.[18] Increased production of stress hormones such as adrenaline, cortisol and glucagon in sepsis neonatorum also plays a role in increasing blood glucose levels.[19] In our study, most suspected sepsis infants had hyperglycemia in 15 infants (30%). In contrast to the study by Campos et al in Brazil reported 99% of 55 patients with neonatal sepsis experienced changes in blood glucose levels, with hypoglycemia being the most common abnormality of 58% .[20] However, our study did not assess the presence or absence of an increase in stress hormones to ensure hyperglycemia caused by sepsis.

Glucose monitoring in urine is a commonly used method for detecting hyperglycemia in NICU patients.[21] Dipstick tests are often used as a daily urine glucose monitoring tool and are more practical with semicualitative or semiquantitative assessments.[22] In our study we found a significant relationship between hyperglycemia and glucosuria in premature infants. In previous studies intravenous glucose administration was associated with the incidence of glucosuria in preterm infants.[23] This is because the kidney threshold for glucose in preterm infants was between 150 to 180 mg / dl and the result of negative glucosuria was not considered to be hyperglycemia.[21] This study is the same as Stonestreet et al. which is found glucosuria with blood sugar levels increased by 152 mg / dl, and supported by the research of Cowet et al, where neonates with glucosuria accompanied by blood sugar levels> 150 mg / dl.[24,25] However, in our study we did not assess the concentration of infusion glucose, nutrition parenteral, steroid drugs given to the subject so that they can be biased in determining the cause of hyperglycemia.

Monitoring glucose in urine is a method commonly used to detect hyperglycemia in NICU patients. The dipstick test is often used as a daily urine

Increased glucose excretion can occur in premature infants with sepsis, intracranial hemorrhage and respiratory distress. These results suggest that clinical instability, with prematurity can contribute to decreased tubular reabsorption of glucose.[9] This is in line with the results of our study where apnoe events were significantly associated with glucosuria .

In our study, there was no relationship between sepsis and glucosuria. The standard gold examination of sepsis is blood culture, of the 13 infants with positive blood cultures found 7 infants (53.8%) found glucosuria. This is also the same as obtained from a study by bekhof 2015 which states that there is no relationship between glucosuria and sepsis which is proven to be a positive blood culture. This is possible due to the fact that glucosuria is only related to gestational age, birth weight and the incidence of slow onset sepsis.

A limitation of our study is the method used only in cross-sectional studies, where data collection was only one time. The number of samples is small and the research flow does not monitor the use of glucose infusion fluids, parenteral nutrition, the use of steroid drugs that affect blood sugar levels, so that it becomes biased. Researchers assume that further research is needed with more sample sizes and cohort methods.

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