

The AST / Platelet Ratio are a Predictor of *Liver Injury* and its Association with Lactic Acid Levels in Pediatric Sepsis Patients Admitted to the Hospital. H. Adam Malik, Medan

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Abstract: *Introduction: Sepsis-associated liver injury (SALI) is one of the main clinical manifestations of sepsis, as well as an independent risk factor for multiple organ dysfunction syndrome and mortality in pediatric sepsis. The early warning biomarkers for identifying SALI remain poorly defined. Objective: To analyze the relationship between aspartate aminotransferase to platelet ratio index (APRI) and Lactate liver injury occurrence in pediatric sepsis, as well as determine the APRI cutoff value for early identification of SALI. Methods: This research is an observational study with a cohort-prospective data collection method. This study took blood samples of patients who were treated at Hospital as many as 26 patients. Samples were examined for AST/Platelet and lactate ratio on days 1 and 3. The study was conducted after obtaining ethical approval and informed consent. Result: 17 boys (73.1%) and 7 girls (26.9%) with the youngest age 1 month and the oldest 17 years. A total of 17 people (65.4%) children showed liver injury. By using the Spearman correlation test, it was shown that there was no significant correlation between APRI and lactic acid on the first day ($p=0,252$) and the third day ($p=0,883$). The results of the analysis using the ROC curve showed that APRI could be used to predict liver injury in pediatric patients with sepsis ($p<0.05$). With APRI cut off day I and day III which are 1.86 and 2,075. Discussion: SALI and lactate is one of the main clinical manifestations of sepsis, an independent risk factor for multiple organ dysfunction syndrome (MODS) and mortality in pediatric sepsis. Conclusions and suggestions: APRI scores can be used to predict liver injury in pediatric patients with sepsis. Further research is needed to outline one by one the factors that contribute to the occurrence of liver injury in pediatric sepsis patients and are associated with PELOD scores to assess mortality of pediatric patients with sepsis.*

Keywords: Sepsis, APRI Score, Lactate, Liver Injury

1. Introduction

Sepsis is life threatening *organ dysfunction*, caused by immune dysregulation against infection. Sepsis is the most common cause of morbidity and mortality in children. . *Sepsis – related liver injury* is one of the major clinical appearances, which is an independent risk factor for multiple organ dysfunction and high mortality rates in pediatric patients with sepsis. *Gold standards* forest abolishing a diagnosis of SALI are an increase in total bilirubin or aspartate aminotransferase (AST) and alanine transaminase (ALT) However, both total bilirubin, AST and ALT can earlier identify the occurrence of injury.

Platelet involvement in sepsis for the occurrence of multi - organ dysfunction with complex and complex processes, through inflammation regulation, tissue integrity, and immune system defenses against infection. Platelets not only act as hemostatic cells, but also play a role in immune defenses and inflammatory processes.⁴

Thus the ratio of aspartate aminotransferase (AST) to platelets (PLT), named as *the AST Platelet Ratio Index* (APRI) is an effective non invasive assessment of liver fibrosis in patients with non - alcoholic fatty liver disease or hepatitis C- related fibrosis. So APRI can potentially provide early warning of SALI in children with sepsis.^{5,6}

The occurrence of lactemia in sepsis is the presence of tissue hypoperfusion, and lactate represents a sign of tissue

hypoxia. In sepsis and SIRS there are known microcirculation disorders that cause tissue hypoxia, and result in organ dysfunction and multiple organ failure.⁷

2. Purpose

This study aims to prove the AST /platelet ratio as an early predictor of *liver injury* and its relationship to lactic acid levels in pediatric sepsis patients treated at H. Adam Malik Medan Hospital.

3. Research Methods

The research was conducted at the Department of Clinical Pathology FK USU / RSUP H. Adam Malik Medan in collaboration with the Department of Children's Health Sciences FK USU / RSUP H. Adam Malik Medan, in March 2021 to July 2021. The sample of study subjects was a pediatric sepsis patient who was treated at H. Adam Malik Medan Hospital, and had met the inclusion criteria and did not meet the exclusion criteria.

The inclusion criteria in this study are pediatric sepsis sufferers according to the National Guidelines of the Indonesian Pediatricians Association Medical Services "Diagnosis and management of sepsis in children.

Examination of Platelets, AST and lactic acid levels on the first and third day is carried out at the Department of Clinical Pathology FK USU / RSUP H. Adam Malik Medan.

Volume 11 Issue 10, October 2022

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Platelet examination using Sysmex XN - 1000The AST examination is performed at the time the sample is taken from the patient with the Automatic Analyzer Architect C 8000, arterial lactate examination using accutrend plus cobas.

4. Statistic Analysis

Data analysis is done using SPSS (Statistical Package for Social Sciences) computer statistics software. A picture of the characteristics on the subject of the study is presented in tabulated form and described. For continuous variables are presented as means \pm SD if the distribution data is normal and as the median if the distribution data is not normal. The Chi - square test is used to compare categorical data. The ROC curve is displayed to see the accuracy of independent risk factors on SALI. To assess the correlation between

APRI and arterial lactate levels, Pearson correlation tests are used when the data is normal. If the data is not normally distributed, spearman rank test is used. All statistical tests with a p value of < 0.05 are considered meaningful.

5. Results

This study was followed by as many as 26 children patients with sepsis who were treated at H. Adam Malik Medan Hospital from March 2021 - July 2021. All selected subjects meet the inclusion criteria. Table 1 displays the characteristics of their search subjects. The most male subjects were 19 (73.1%). The average age of the child subjects involved in the study was 8.2 years with the youngest age being 0.08 years (1 month) and the oldest being 17 years old. A total of 17 people (65.4%) of children showed liver injury.

Table 1: Characteristics of Research Subjects

Characteristics of the Subject	n = 26
Gender, n (%)	
Man	19 (73, 1)
Woman	7 (26, 9)
Age, year	
Average (SD)	8, 20 (7, 15)
Median (Min - Mak)	10, 50 (0, 08 - 17)
Liver injury, n (%)	
Yes	17 (65, 4)
Not	9 (34, 6)

Table 2: Laboratory Characteristics on Examination of Days I and III

Characteristic Laboratory	Day I	Day III	p*
Platelets, thousand cells/ μ L			
Average (SD)	102, 73 (20, 22)	67, 35 (27, 62)	$<0, 001$
Median (Min - Mak)	99 (86 - 194)	65, 50 (22 - 163)	
AST, IU/L			
Average (SD)	231, 89 (32, 66)	314 (79, 99)	0, 001
Median (Min - Mak)	210, 50 (200 - 287)	310 (84 - 457)	
ALT, IU/L			
Average (SD)	158, 19 (7, 86)	221 (98, 10)	$<0, 001$
Median (Min - Mak)	156, 50 (150 - 178)	195, 50 (90 - 667)	
Lactic Acid, mmol/L			
Average (SD)	2, 59 (0, 30)	2, 92 (1, 13)	0, 450
Median (Min - Mak)	2, 50 (2, 10 - 3, 20)	3, 25 (0, 60 - 5, 10)	
Total Bilirubin			
Average (SD)	10, 48 (2, 72)	13, 15 (3, 18)	0, 002
Median (Min - Mak)	10, 41 (5, 23 - 16, 80)	12, 11 (10, 41 - 19, 78)	
APRI			
Average (SD)	4, 84 (3, 38)	9, 81 (8, 09)	$<0, 001$
Median (Min - Mak)	6, 06 (0, 59 - 9, 59)	11, 05 (0, 64 - 29, 95)	

*Wilcoxon

Almost all parameters showed significant differences in average or median values between the first day of examination and the third day of treatment, except for lactic acid levels.

Correlation of APRI with Lactic Acid on Day One and Day Three

Tables 3 and 4 show the results of the correlation analysis of APRI and lactic acid on the first day and the third day of treatment. Using spearman correlation tests, it showed that no significant correlation was found between APRI and lactic acid on the day I ($p=0.067$) and day III ($p=0.727$)

Table 3: Correlation of APRI with Lactic Acid on Day I

APRI	Lactic Acid
	n = 26
	p = 0.067
	r = - 0.365

Table 4: Correlation of APRI with Lactic Acid on Day III

APRI	Lactic Acid
	n = 26
	p = 0.727
	r = - 0.072

Characteristic Relationship of Subjects and Laboratories to Liver Injury

Table 5 showed the results of an analysis of the characteristic relationship of subjects to *liver injury* in children with sepsis, showing a significant absence of a relationship between sex and age to the incidence of *liver injury* ($p > 0.05$).

In table 6, platelet levels of the first day in subjects of children with *liver injury* showed a median value of 97 thousand cells / μL while in the group of children without *liver injury* showed a higher median of 106 thousand cells / μL . Using mann Whitney test showed a significant association between platelets and *liver injury* ($p = 0.002$).

APRI levels on the first day (table 6) in subjects of children with *liver injury* showed an average value of 7.05 while in the group of children without *liver injury* showed a lower average of 0.66. Using the *Independent T* test, there was a significant association between first - day APRI and *liver injury* ($p < 0.0001$).

APRI levels on day three (table 7) in subjects of children with *liver injury* showed an average value of 14.67 while in the group of children without *liver injury* showed a lower average of 0.71. Using the *Independent T* test showed there was a significant association between third - day APRI and *liver injury* ($p < 0.001$).

Table 5: Characteristic Relationship of Subjects to Liver Injury

Characteristics of the Subject	Liver Injury (+) n = 17	Liver injury (-) n = 9	P
Gender, n (%)			
Man	12 (63, 2)	7 (36, 8)	1, 000 ^a
Woman	5 (71, 4)	2 (28, 6)	
Age, year			
Average (SD)	6, 48 (6, 99)	11, 46 (6, 6)	0, 266 ^b
Median (Min - Mak)	1 (0, 08 - 16)	14 (0.08 - 17)	

^aFischer's Exact, ^bMann Whitney

Table 6: Relationship of Laboratory Parameters Day I to Liver Injury

Laboratory parameters	Liver Injury (+) n = 17	Liver injury (-) n = 9	P
Platelets day I, thousand cells/ μL			
Average (SD)	100, 94 (24, 84)	106, 11 (4, 91)	0, 002 ^a
Median (Min - Mak)	97 (86 - 194)	106 (100 - 112)	
AST day I, IU/L			
Average (SD)	232, 29 (34, 73)	231, 11 (30, 34)	0.663 ^a
Median (Min - Mak)	210 (200 - 287)	211 (204 - 280)	
ALT day I, IU/L			
Average (SD)	158, 29 (7, 52)	158 (8, 94)	0, 930 ^b
Median (Min - Mak)	157 (150 - 178)	155 (150 - 178)	
Lactic Acid day I, mmol/L			
Average (SD)	2, 35 (0, 34)	2, 7 (0, 17)	0, 073 ^a
Median (Min - Mak)	2, 4 (2, 1 - 3, 2)	2, 8 (2, 5 - 2, 9)	
Total Bilirubin day I			
Average (SD)	10, 69 (2, 72)	10, 09 (2, 84)	0.605 ^b
Median (Min - Mak)	10, 41 (5, 4 - 16, 8)	10, 41 (5, 23 - 16, 18)	
APRI day I			
Average (SD)	7, 05 (1, 67)	0, 66 (0, 03)	<00.001 ^b
Median (Min - Mak)	6, 94 (3, 03 - 9, 59)	0, 66 (0, 59 - 0, 69)	

^aMann Whitney, ^bT Independent

Table 7: Relationship of Laboratory Parameters Day III to Liver Injury

Laboratory parameters	Liver Injury (+) n = 17	Liver injury (-) n = 9	P
Platelets day III, thousand cells/ μL			
Average (SD)	66, 35 (21, 6)	69, 22 (38, 02)	0, 434 ^a
Median (Min - Mak)	66 (22 - 115)	53 (40 - 163)	
AST day III, IU/L			
Average (SD)	320, 47 (80, 63)	301, 78 (82, 06)	0.808 ^a
Median (Min - Mak)	310 (84 - 457)	311 (110 - 387)	

ALT day III, IU/L			
Average (SD)	230, 24 (115, 14)	203, 56 (55, 11)	0.850 ^a
Median (Min – Mak)	196 (180 - 667)	195 (90 - 278)	
Lactic Acid day III, mmol/L			
Average (SD)	3, 23 (0, 92)	2, 34 (1, 31)	0, 401 ^a
Median (Min – Mak)	3, 3 (1 - 5, 1)	1, 8 (0, 6 - 3, 9)	
Total Bilirubin day III			
Average (SD)	13, 92 (3, 44)	11, 69 (2, 09)	0, 174 ^a
Median (Min – Mak)	12, 11 (10, 41 - 19, 78)	10, 43 (10, 41 - 16, 8)	
APRI day III			
Average (SD)	14, 63 (5, 57)	0, 71 (0, 05)	<00.001 ^b
Median (Min – Mak)	13, 1 (3, 38 – 25, 95)	0, 7 (0, 64 – 0, 77)	

^aMann Whitney, ^bT Independent

Analysis of APRI and Lactic Acid Day I as well as APRI and Lactic Acid Day III in Predicting Liver Injury in Pediatric Patients with Sepsis

The results of the analysis using the ROC curve (figure 1) obtained widely AUC from APRI day one in predicting liver injury in pediatric patients with sepsis is by 100% with a p value of <0.001 and 95% IK 100% - 100%. This suggests that APRI on the first day may be used to predict liver injury in pediatric patients with sepsis (p<.001). Based on the line graph in figure 2, the first day's APRI level cut value to predict *Liver Injury* is 1.86.

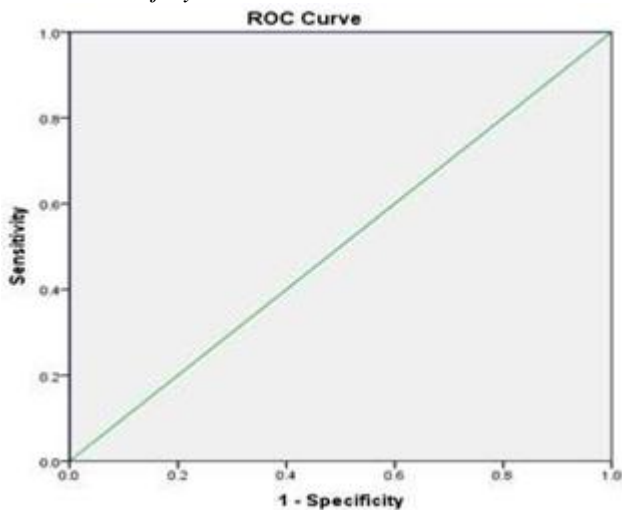


Figure 1: First Day's ROC APRI Curve against *Liver Injury* in Pediatric Patients with Sepsis

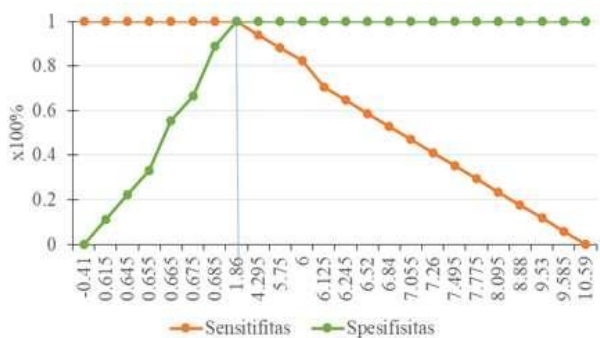


Figure 2: Graphics of Sensitivity and Specificity Lines of First Day APRI Levels against *Liver Injury*

Using the first day APRI *cut off* value of 1.86 to predict the severity of the disease, obtained sensitivity value of 100%, specificity of 100%, positive guess value of 100%, negative suspect value of 100%, accuracy of first day APRI levels is

100%.

The results of the analysis using the ROC curve (figure 3) obtained widely AUC from lactic acid the first day in predicting *liver injury* in pediatric patients with sepsis is 71.6% with a value of p=0.075 and 95% IK 51.7% - 91.4%. This suggests that lactic acid on the first day cannot be used to predict *liver injury* in pediatric patients with sepsis (p>0.05).

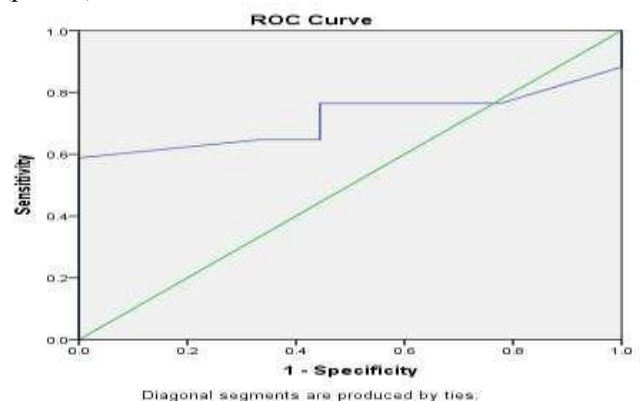


Figure 3: First Day's ROC Curve of Lactic Acid against *liver injury* in Pediatric Patients with Sepsis

The results of the analysis using the ROC curve (figure 4) obtained widely AUC from APRI day three in predicting *liver injury* in pediatric patients with sepsis is by 100% with a p value of < 0.001 and 95%IK 100% - 100%. This suggests that APRI on the third day may be used to predict *liver injury* in pediatric patients with sepsis (p <.001). Based on the line graph in figure 5, the third day's APRI level cut off value to predict *liver injury* is 2, 075.

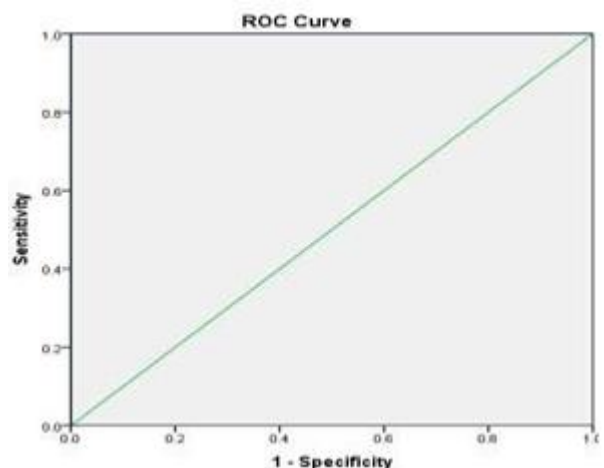


Figure 4: Third Day's ROC APRI Curve to *Liver Injury* in Pediatric Patients with Sepsis

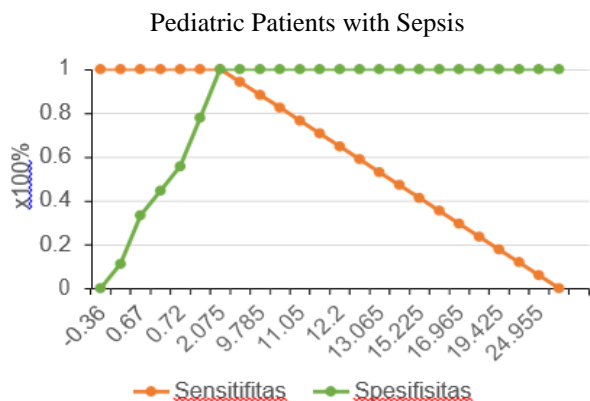


Figure 5: Sensitivity Line Graph and Specificity of Third Day APRI Levels to Liver Injury

By using the third day APRI *cut off* value of 2, 075 to predict liver injury, obtained sensitivity value of 100%, specificity of 100%, positive guess value of 100%, negative guess value of 100%, Accuracy of third day APRI levels is 100%. The results of the analysis using the ROC curve (figure 6) obtained widely AUC from Lactic Acid day three in predicting liver injury in pediatric patients with sepsis is by 60.1% with a value of $p = 0.403$ and 95%IK 34.2 % - 86.1%. This suggests that lactic acid on the third day cannot be used to predict liver injury in pediatric patients with sepsis ($p > 0.05$).

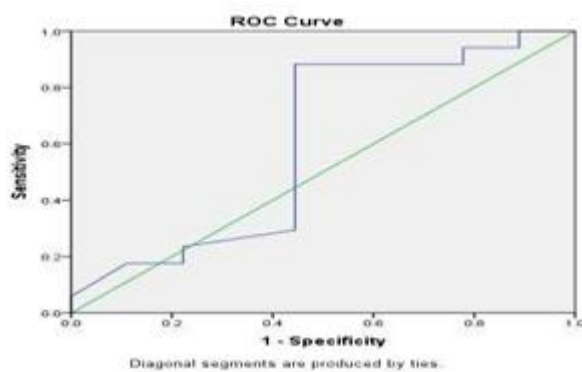


Figure 6: Third Day of Lactic Acid ROC Curve to Liver Injury in Pediatric Patients with Sepsis

6. Discussion

The most male subjects were 19 (73.1%). The average age of the child subjects involved in the study was 8.2 years with the youngest age being 0.08 years (1 month) and the oldest being 17 years old. A total of 17 people (65.4%) of children showed liver injury. Unlike the study conducted by Hirani et al, 2019. A total of 325 children were analyzed during the study period. Of these 58.8% were women, the average age was 8 months. Septic shock was diagnosed in 50 of the 325 children in care, giving it a prevalence of 15.4%. The average age was 4 months, neonates at 25.6% and infants at 20.9% made up the highest proportion of children with septic shock. None of the children over the age of >60 months were diagnosed with septic shock.⁸

But in line with the Gosai et al study also obtained such results, of 455 infants or children diagnosed sepsis, 278 (61.10%) were male, the rest were female. The corresponding results were also reported by Kumar et al and

Verna et al who found the number of sepsis patients in infants or boys more frequently than female ones.⁹

Male sex is said to be one of the risk factors for sepsis in children. Male children are more sensitive to adverse perinatal and postnatal environmental conditions, and more likely to be born for example with premature conditions with lower birth weight (BBLR); Both of these are also risk factors for sepsis in infants or children. The condition is influenced by the regulatory factors of gammaglobulin synthesis located on the X chromosome. Males have only one X chromosome while females have two X chromosomes; This makes immunological protection in male infants lower than in females.

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Some factors that play a role in sepsis mortality in children include factors, causative microorganisms, early diagnosis, and the procedures given. The incidence of sepsis is significantly higher in younger age groups and children with comorbidities resulting in immune deficiency states, such as malignancy, transplantation, chronic diseases, and congenital heart abnormalities. The most common cause of sepsis infection in children, namely respiratory tract infections, followed by non-specific infections, bacteremia, urinary tract infections, gastrointestinal infections, central nervous system infections, and others. Surgical wound infections and soft tissues can also cause sepsis in children.¹⁰

In this study, 17 people (65.4%) of children showed liver injury. Higher hospital deaths in the liver injury group suggest that liver injury correlates with the prognosis of sepsis, which is consistent with previous research, a study conducted by Nessler et al 2016 showed that the incidence of liver injury in adults was 74.7% (156/449) and the mortality of adult patients with sepsis with complications of serum TBIL >2.0 mg/dL was 42%. According to our current results, the incidence and death of liver injury in pediatric patients is relatively lower than in adult patients. Given that age affects the assessment of liver injury, it is important to investigate specific predictors for early identification of liver damage in pediatric patients with sepsis.¹¹

Almost all parameters showed significant differences in average or median values especially the liver fail between the first day and the third day of treatment, except for lactic acid levels. Research conducted by Shah et al found that sepsis (n=123) is the most common cause of increased liver enzymes One of the manifestations of liver dysfunction due to sepsis is sepsis-induced cholestasis, and elevated levels of SGOT, SGPT and bilirubin can be found in this condition.¹¹

Liver dysfunction is one of the components of MODS and is usually a marker of poor prognosis. The liver plays an important role in a variety of metabolic activities, homeostasis, and devotees' defenses. Liver dysfunction is generally seen only as a consequence of shock and early tissue hypoperfusion, but in fact injury to the liver is one of the major factors in the onset and amplification of multiple organ failure. Average liver dysfunction in pediatric patients with sepsis was 39.9%, lower than the incidence of disorders

in other sepsis - related organs such as the lungs, kidneys, brain, cardiovascular, etc. However, dysfunction and liver failure are associated with severe complications in sepsis patients.¹²

Mortality rates in pediatric patients with sepsis who experience sepsis - related liver dysfunction range from 54% - 68%, higher than sepsis patients with respiratory disorders. This data proves that the liver plays an important role in the survival and recovery of patients after sepsis injury. Khalil et al in a prospective observational study conducted on 153 infants and children who were proven to be sepsis based on blood cultures found that liver dysfunction is very common in early sepsis in infants or children, most often in the form of cholestatic jaundice (42.5%) and alanineamino transferase (ALT) which increased by 37.3%.¹³

Research conducted by Han et al found the prevalence of cholestasis in sepsis in infants at 38.9%. Cholestasis in sepsis occurs due to impaired bile acid transport function, the release of microbial products such as bacterial endotoxins results in the activation of proinflammatory cytokines that inhibit the transport of organic anions in sinusoids and hepatocyte canal membranes. This interferes with the function of hepatocytes in the use and excretion of bile acids, causing damage to liver cells due to the retaining of materials that should be secreted into the duodenum.¹⁴

Han et al showed that average levels of AST, ALT, Bilirubin, LDH and γ GT in 91 infants shown cholestasis in sepsis were in the normal range at the beginning of cholestasis. SGOT is not only found in liver tissue but also in other tissues such as the heart, kidneys, striated muscles, and an increase in SGOT in infant or child sepsis can be associated with an excess inflammatory reaction that then results in hepatocellular injury.¹⁴

Tables 3 and 4 show the results of the correlation analysis of APRI and lactic acid on the first day and the third day of treatment. Using spearman correlation tests, it showed that no significant correlation was found between APRI and lactic acid on the first day ($p=0.067$) and day three ($p=0.727$). In the results of our study did not find a significant association, this is due to several factors, among others we do not describe other factors that play a role in *liver injury* in pediatric patients with sepsis, the use of APRI and lactic acid scores are only 2 factors that we use as a benchmark to predict the occurrence of *liver injury* in pediatric patients with sepsis.

If associated with lactic acid with the occurrence of *liver injury*, the results of our study are not in line with the research conducted by Dou et al, 2019. They found that there was a meaningful association of lactic acid levels between pediatric patients who only had sepsis compared to pediatric patients who had sepsis but also had *liver injury*. ($p<0.05$).¹⁵ But if viewed in relation to the APRI score of our study is different from the results of a study conducted by Dou et al, 2019 also reported that in his study the APRI score as an independent factor for the occurrence of *liver injury* in pediatric patients with sepsis.¹⁵

In addition, aspartateaminotransferase (AST) to PLT ratio,

referred to as APRI, is an effective noninvasive examination of liver fibrosis in patients with non - alcoholic, fatty liver disease or hepatitis C - related fibrosis. Either cirrhosis of the liver or liver fibrosis is closely related to liver dysfunction and the initial inflammatory processes that trigger liver injury. We hypothesize that the AST/PLT ratio index may provide the potential for early warning of liver injury in children with sepsis. Early introduction of liver injury is essential for timely management for patients with sepsis to prevent the occurrence of MODS, which remains a challenge in ICU.¹⁵

PLT is involved in sepsis in the liver's response to early sepsis and plays a key role in hepatocyte injury through interaction with neutrophils, Kuffer cells, and endothelial cells. Platelet aggregation that occurs due to endothel dysfunction, this leads to TF activation and activation of coagulation and platelet pathways. This activation causes the cell T to differentiate into Th1 (Th1) T cells and Th2 (Th2) T cells. Th1 cells secrete pro-inflammatory cytokines such as Tumor Necrosis Factor (TNF), interferon γ (IFN - γ), interleukin 1 - β (IL - 1 β), IL - 2, IL - 6 and IL - 12. Cell Th2 secretes anti-inflammatory cytokines such as IL - 4, IL - 10, and IL - 13. The formation of pro-inflammatory cytokines is maintained in the sinusoids of the liver causing the liver to experience dysfunction, in addition sepsis also leads to the possibility of excessive use of platelets.¹⁶

In other aspects, AST is an enzyme, especially those in hepatocytes. Intracellular AST is released into the circulatory system when the hepatocytes must be injured. Currently, AST is a widely accepted clinical marker for liver injury. The usual liver function test to measure liver damage is the liver function test. Abnormalities of liver enzymes such as serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) that increased twice the normal limit can be found in patients with neonatal sepsis who experience liver dysfunction. Research conducted by Adiga et al showed lower levels of SGOT (AST) in women than in men. Variations in differences in liver enzyme results in both sexes are often associated with hormonal factors.¹⁷

Xu et al in his research aimed at knowing the levels of TNF - α and IL - 6 against the incidence of acute liver failure in patients with sepsis neonatorum awitan early (SNAD), found that levels of TNF - α and IL - 6 were positively correlated with SGOT, SGPT, and SGOT/SGPT ratios in early-onset awitan neonatorum sepsis. Neonatorum sepsis patients more often experienced an increase in SGOT of 71.8%. SGOT (AST) is not only found in the liver tissue, therefore the increase in SGOT (AST) in neonatal sepsis first occurs in SGPT.¹⁸

Liver dysfunction is one of the rare components of multiple organ dysfunction syndrome, SGPT itself is one of the specific liver examination biomarkers because it specifically has a high concentration in hepar and very low concentration in other tissues.¹⁸ Dinar shanty et al in terms of sepsis and impaired liver function state that at the time of sepsis there will be micro-circulatory and systemic disorders, as well as the release of proinflammatory cytokines, reactive oxygen species (ROS) and nitric oxide (NO) by Kupffer cells, then

neutrophils recruited in the liver also produce proinflammatory cytokines. This will induce and result in further damage to the liver's sinusoid endothelial cells as well as hepatocytes. Clinical manifestations of impaired liver function in sepsis can be hypoxic hepatitis or cholestasis. In hypoxic hepatitis there will be AST and ALT leaks that signal acute mitochondrial and cell injury.¹⁹

The results of the analysis using the ROC curve (figure 1) obtained widely AUC from APRI day one in predicting liver injury in pediatric patients with sepsis is by 100% with a p value of <0.001 and 95% IK 100% - 100%. This suggests that APRI on the first day can be used to predict liver injury in pediatric patients with sepsis (p <.001) and based on the line graph in figure 2 then obtained a cut off value of the first day's APRI levels to predict liver injury is 1.86

The results of the analysis using the ROC curve (figure 3) obtained widely AUC from Lactic Acid the first day in predicting liver injury in pediatric patients with sepsis were 71.6% with a value of p=0.075 and 95% IK 5 1.7% - 91.4%. This suggests that Lactic Acid on the first day cannot be used to predict liver injury in pediatric patients with sepsis.

The results of the analysis using the ROC curve (figure 4) obtained widely AUC from APRI day three in predicting liver injury in pediatric patients with sepsis is by 100% with a p value of < 0.001 and 95% IK 100% - 100%. This suggests that APRI on day three can be used to predict liver injury in pediatric patients with sepsis (p <.001) and based on the line graph in figure 5 then obtained a third - day APRI level cut off value to predict liver injury is 2, 075.

The results of the analysis using the ROC curve (figure 6) obtained widely AUC from Lactic Acid day three in predicting liver injury in pediatric patients with sepsis is by 60.1% with a value of p = 0.403 and 95% IK 34.2 % - 86.1%. This suggests that Lactic Acid on the third day cannot be used to predict liver injury in pediatric patients with sepsis (p > 0.05). The results of the analysis used the ROC curve, where the first day and third day APRI scores in our study matched the results of the study conducted by Dou et al 2019. The ROC analysis for APRI as a nearly warning bio marker of liver injury with are as below the curve (AUC) was 0.889 (95% IK: 0.851 - 0.927), while in our study it was 1.00 (95% IK: 1.00 - 1.00).

7. Conclusion

The results of the analysis using the ROC curve obtained widely AUC from APRI the first day and the third day is 1.00 so that it can be used as a predictor of liver injury with the value of the first day cut off of 1.86 and the third day of 2.075.

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