Clinical Nutrition ESPEN 34 (2019) 81–86

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

Incidence and risk factors of parenteral nutrition-associated liver disease in hospitalized adults: A prospective cohort study

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ARTICLE INFO

Article history:
Received 9 April 2019
Accepted 26 August 2019

Keywords:
PNALD
Liver injury
Parenteral nutrition
Incidence
Risk factor

SUMMARY

Background and aims: Parenteral nutrition-associated liver disease (PNALD) is a common complication in patients receiving parenteral nutrition (PN). Few studies have investigated the incidence and risk factors of PNALD in adult patients receiving PN with newer generation intravenous lipid emulsions. The aim of this study was to investigate the incidence and risk factors of PNALD in hospitalized adult patients.
Methods: Patients expected to receive PN for more than 14 days and have normal liver tests at baseline during September 2016 to February 2017 were enrolled. All patients were followed until there were liver test abnormalities. Incidence, onset and characteristics of PNALD, calories intake, amount of fat and carbohydrate, types of fat, nutrition status, and incidence of infection were evaluated.
Results: Forty-four adults were recruited. The incidence of PNALD was 59.1% (22.7% steatosis, 34.1% cholestasis, and 2.3% mixed type). Median onset of PNALD was 12.5 days (range: 4–42) and the onset was not significantly different between each subtype. In multiple regression analysis, severe malnutrition and amount of carbohydrate were independent risk factors for PNALD with an odds ratio of 13.25 (95% CI: 1.37–128.24; $p = 0.026$) and 21.61 (95% CI: 1.81–258.56; $p = 0.015$), respectively.
Conclusions: PNALD was common in this group of patients. In contrast to previous studies, cholestasis was more common than steatosis, and the median onset was not different between each subtype. In severely malnourished patients, physicians need to exercise caution and monitor for PNALD intensively, and overfeeding of carbohydrate should be avoided to prevent PNALD from occurring.

1. Introduction

Parenteral nutrition (PN) is a life-saving therapy in patients with inadequate bowel function. However, it is associated with many complications, including hyperglycemia, electrolytes abnormalities, catheter-related infection, and parenteral nutrition-associated liver disease (PNALD). PNALD is commonly reported in patients receiving PN with the incidence rate of 25%–100%, and it can increase morbidity and mortality in these patients [1,2]. The exact cause of this condition remains unclear and seems to be multifactorial [1,3]. Risk factors of PNALD are divided into two main groups. The first group is nutrition-related risk factors such as overfeeding, types of intravenous lipid emulsion (ILE), and nutritional deficiencies. The other group is patient-related risk factors, including sepsis, lack of enteral intake, and length of short bowel remnant [1,2,4,5]. PNALD is diagnosed by excluding other non-PN causes of liver injuries in patients with PN therapy [3,6].

Previous studies assessed the incidence and risk factors of PNALD in children and patients receiving home PN. Consequently, most of the recommendations of PNALD management, especially nutritional factors, are extrapolated from these groups of patients. PNALD in hospitalized adults receiving short-term PN is different from patients who are on long-term PN. PNALD in long-term PN presents mainly as chronic manifestation of liver injuries and can progress to severe fibrosis and chronic liver failure [4,7], while PNALD in short-term PN is usually acute and is potentially reversible after withdrawing PN therapy [8]. Even though liver injuries can be reversed, it is one of the causes for early PN termination that results in inadequate nutritional treatment [9]. In addition, some risk factors of PNALD, such as catheter-related bloodstream

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https://doi.org/10.1016/j.clnesp.2019.08.009
2405-4577/

infection (CRBSI) and short length of bowel, are more common in long-term PN [10]. There are few studies about PNALD in adults admitted to acute care setting. As a result, incidence and risk factors of PNALD in this group of patients are needed to be explored.

A recent study on PNALD in hospitalized adult patients did not perform a liver imaging, therefore, other possible causes of liver injuries such as biliary obstruction could not be excluded [8]. Additionally, PN with newer generation ILE such as Clinoleic® and SMOF lipid® have been developed, and they may help to prevent and treat PNALD [11]. Consequently, the incidence, clinical characteristics, and risk factors of PNALD could change because of this advancement.

The aim of this study was to identify the incidence of PNALD in hospitalized adult patients. Both nutrition-related and patient-related risk factors contributing to PNALD were also evaluated in this group of patients.

2. Materials and methods

2.1. Patients

This was a prospective cohort study in adult patients who were admitted to the King Chulalongkorn Memorial Hospital (KCMH) (Bangkok, Thailand) from September 2016 to February 2017. Patients aged 18 years or more who were expected to receive PN for at least 14 days were enrolled. Patients who had a history of liver diseases, abnormal liver tests and PN termination before 14 days without having any abnormalities of liver tests were excluded. The protocol for this study was approved by the Institutional Review Board (IRB; number 465/59) of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

2.2. Study design

Patients with normal baseline liver tests before starting PN were included in the study. Liver tests were regularly monitored at least once a week until there were abnormal liver tests or discontinuance of PN. Patients who stopped PN before 14 days without any abnormal liver tests were excluded to reduce false negative rate that can affect the incidence of PNALD [12]. The liver injuries were divided into 3 groups: 1. steatosis with aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 1.5 times of the normal value, 2. cholestasis with direct bilirubin (DB) > 2 mg/dL and alkaline phosphatase (ALP) > 1.5 times of the normal value [3,4,12], and 3. mixed type having both steatosis and cholestasis characteristics with R-value (serum ALT/upper limit of normal (ULN) divided by serum ALP/ULN) between 2 and 5. If the R-value was more than 5 or less than 2, liver abnormalities were classified as steatosis and cholestasis, respectively [13]. In all patients with liver injuries, the non-PN causes of liver diseases including viral hepatitis (A, B, C), drugs and toxins, ischemic hepatitis, and biliary obstruction, were excluded by medical chart review, laboratory examination, and abdominal ultrasound. The following data were collected: sex, age, weight, height, body mass index (BMI), nutritional status by subjective global assessment (SGA), follow-up time, incidence of liver dysfunction, onset of PNALD, amount of energy, amount of carbohydrate, amount and type of fat, incidence and type of infection.

In the study, all patients received PN via central venous catheter and a continuous infusion pump. Commercial total nutrient admixtures (TNA) were used and the PN bag was changed every 24 h. In our hospital, lipids in TNA were administered as 20%Clinoleic® or 20%SMOF lipid®, depending on the patient's requirement and clinicians' preference. Clinoleic® consists of 80% olive oil and 20% soy oil, omega-6 fatty acid 1.4–2.2 g/100 mL and phytosterol 227–274 mg/L. SMOF lipid® consists of 30% soy oil, 30% medium-chain triglycerides, 25% olive oil, and 15% fish oil, omega-6 fatty acid 2.85 g/100 mL and phytosterol 179–207 mg/L. TNA with 20% Intralipid® was not available in our hospital.

2.3. Statistical analysis

Data were analyzed using SPSS Statistics version 17 (SPSS, Inc., Chicago, IL, USA). Differences in clinical characteristics and risk factors of PNALD were analyzed by Pearson's chi-square for categorical parameters and independent samples t-test for continuous data. Risk factors for PNALD were also evaluated and identified using simple and multiple logistic regression analysis. The test of multicollinearity was evaluated by the variance inflation factors (VIF), which VIF greater than 5 represented critical levels of multicollinearity. Data are shown as number, number and percentage, mean ± standard deviation, median and range, or median and interquartile range. A p-value of less than 0.05 was regarded as being statistically significant.

3. Results

3.1. Patient characteristics

Sixty patients met the inclusion criteria during the study period; however, 16 patients were excluded because PN was stopped before 14 days and there were no abnormalities of the liver tests. Hence, 44 patients, 21 men (47.7%) and 23 women (52.3%), were enrolled into the study. The mean age of the patients was 61.6 ± 13.4 years and the mean BMI was 20.6 ± 4.2 kg/m^2. All patients had malnutrition diagnosed by SGA, with 38.6% had moderate malnutrition (SGA B) and 61.4% had severe malnutrition (SGA C). The most common indication for PN was inadequate enteral nutrition (81.8%). The median follow-up time was 14 days (range 4–42). Infection occurred in 34.1% of the patients. The most common type of infection was CRBSI (11.4%). Patients' characteristics are shown in Table 1.

3.2. Incidence and characteristics of PNALD

Overall, 26 patients developed abnormal liver tests during the monitoring period. The possible causes of liver diseases, including viral hepatitis, drugs and toxins, ischemic hepatitis, and biliary obstruction, were evaluated and 25 patients had negative results. One patient had positive hepatitis B surface antigen. However, hepatitis B viral load was undetectable (<10 IU/mL), and anti-hepatitis B e-antigen was positive. Ultrasound showed no liver abnormality. Hence, the patient was most likely diagnosed with inactive chronic hepatitis B infection; it was less likely to be the cause of having an abnormal liver test.

Overall, the incidence of PNALD in patients who received PN was 59.1% (26/44 patients). 22.7% (10/44 patients) had steatosis subtype, 34.1% (15/44 patients) had cholestasis subtype, and 2.3% (1/44 patients) had mixed subtype.

The median onset of abnormal liver tests after receiving PN was 12.5 days (range: 4–42). For each subtype of PNALD, steatosis occurred at the median of 13 days (range: 4–42), cholestasis had the median onset of 12 days (range: 6–31), and mixed type occurred 19 days after PN. There was no significant difference between the onset of PNALD between each subtype ($p = 0.744$). With regards to the characteristics of the liver tests, the steatosis group had mean AST 52.5 ± 15.2 U/L and ALT 65.7 ± 19.4 U/L, which were 1.75 times and 2.2 times higher than the upper limit of the normal value, respectively. In the group of cholestasis, the mean ALP was 204.6 ± 106.9 U/L, which was 1.7 times higher than the upper limit

Table 1
Characteristics of the study population.

Factors	No PNALD (n = 18)	PNALD (n = 26)	Total (n = 44)
Sex			
Male	6 (33.3%)	15 (57.7%)	21 (47.7%)
Female	12 (66.67%)	11 (42.3%)	23 (52.3%)
Age			
Mean ± SD, Years	60.8 ± 14.7	62.0 ± 12.7	61.6 ± 13.4
Weight			
Mean ± SD, Kg	52.9 ± 12.3	53.5 ± 14.4	53.3 ± 13.4
Height			
Mean ± SD, cm	158.5 ± 9.9	161.6 ± 8.7	160.3 ± 9.2
BMI			
Mean ± SD, kg/m^2	21.0 ± 4.0	20.4 ± 4.3	20.6 ± 4.2
Nutrition status			
SGA B	12 (66.7%)	5 (19.2%)	17 (38.6%)
SGA C	6 (33.3%)	21 (80.8%)	27 (61.4%)
Indication for PN			
Gut obstruction	2 (11.1%)	5 (19.2%)	7 (15.9%)
Inadequate EN	16 (88.9%)	20 (76.2%)	36 (81.8%)
Short bowel syndrome	0 (0%)	1 (3.8%)	1 (2.3%)
Follow-up time			
Median (range), Days	16.5 (14–39)	12.5 (4–42)	14 (4–42)
Infection	Total Infection 2 (11.1%) - CRBSI 1 (5.6%) - UTI 1 (5.6%)	Total Infection 13 (50.0%) - CRBSI 4 (15.4%) - Intraabdominal infection 3 (11.5%) - Pneumonia 3 (11.5%) - UTI 1 (3.8%) - CNS infection 1 (3.8%) - Cellulitis 1 (3.8%)	Total Infection 15 (34.1%) - CRBSI 5 (11.4%) - Intraabdominal infection 3 (6.8%) - Pneumonia 3 (6.8%) - UTI 2 (4.5%) - CNS infection 1 (2.3%) - Cellulitis 1 (2.3%)

Abbreviations: PNALD, parenteral-related liver disease; SD, standard deviation; BMI, body mass index; SGA, subjective global assessment; PN, parenteral nutrition; EN, enteral nutrition; CRBSI, catheter-related blood stream infection; UTI, urinary tract infection; CNS, central nervous system.

of the normal value, and TB was 2.4 ± 1.0 mg/dL. One patient with mixed type had AST 92 U/L, ALT 98 U/L, ALP 186 U/L, and TB 2.7 mg/dL (R-value = 2.1). The most common finding from abdominal ultrasound was normal hepatobiliary systems (92.3%). Ultrasonographic finding of fatty liver was found in only 2 patients (7.7%): 1 patient from the steatosis group and 1 patient from the mixed group. Gallbladder stones/sludge was not found in any patients. The summation of the data are shown in Table 2.

3.3. Risk factors of PNALD

The risk factor for developing PNALD was severe malnutrition assessed by SGA (SGA C). Severe malnutrition was significantly higher in patients with PNALD than patients without PNALD ($p = 0.001$). Other risk factors such as mean energy (34.2 kcal/kg/day vs. 25.9 kcal/kg/day, $p = 0.006$), mean carbohydrate (3.1 g/kg/day vs. 5 g/kg/day, $p = 0.001$), and mean fat (0.9 g/kg/day vs. 1.3 g/kg/day, $p = 0.001$) were also significantly higher in patients with PNALD. In addition, infection was more common in patients with PNALD ($p = 0.006$). However, types of ILE were not significantly different between those with PNALD and those without PNALD ($p = 0.858$) (Table 3).

Data from the simple logistic regression analysis showed that patients with severe malnutrition by SGA had a significantly higher risk for developing PNALD, with an odds ratio of 8.4 (95% CI: 2.11–33.48; $p = 0.003$). Additionally, infection was also a significant risk factor for PNALD with an odds ratio of 8 (95% CI: 1.52–42.02; $p = 0.014$). As for nutrition-related risk factors, patients receiving higher amount of energy, carbohydrate, and fat were significantly associated with higher risk of developing PNALD, with an odds ratio of 1.11 (95% CI: 1.02–1.20; $p = 0.013$), 4.21 (95% CI: 1.79–9.89; $p = 0.001$), and 178.3 (95% CI: 7.42–4282.8; $p = 0.001$), respectively (Table 4).

Test for multicollinearity was done by VIF method, and there was a collinearity in the amount of fat (VIF = 5.06). To decrease the collinearity, the amount of fat was divided into 2 groups, <1 g/kg/

Table 2
Onset and characteristics of the different subtypes of PNALD.

Factors	All PNALD (n = 26)	Steatosis (n = 10)	Cholestasis (n = 15)	Mixed (n = 1)
Onset				
Median (range), Days	12.5 (4–42)	13 (4–42)	12 (6–31)	19
AST				
Mean ± SD, U/L	49.7 ± 25.2	52.5 ± 15.2	47.7 ± 31.2	92.0
ALT				
Mean ± SD, U/L	58.5 ± 23.6	65.7 ± 19.4	54.3 ± 26.3	98.0
ALP				
Mean ± SD, U/L	163.6 ± 96.6	104.8 ± 37.5	204.6 ± 106.9	186.0
DB				
Mean ± SD, mg/dL	1.8 ± 1.1	0.9 ± 0.5	2.4 ± 1.0	2.7
Ultrasound results	- Normal 24 (92.3%) - Fatty liver 2 (7.7%)	- Normal 9 (90%) - Fatty liver 1 (10%)	- Normal 15 (100%)	- Fatty liver 1 (100%)

Abbreviations: PNALD, parenteral nutrition-related liver disease; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; DB, direct bilirubin; SD, standard deviation.

Table 3
Risk factors for PNALD.

Factors	No PNALD (n = 18)	PNALD (n = 26)	*p* value
Nutritional status			
SGA B	12 (66.7%)	5 (19.2%)	**0.001**
SGA C	6 (33.3%)	21 (80.8%)	
Energy			
Mean ± SD (kcal/day)	1336.9 ± 414.8	1737.1 ± 366.0	**0.002**
Mean ± SD (kcal/kg/day)	25.9 ± 8.8	34.2 ± 9.7	**0.006**
Carbohydrate			
Mean ± SD (g/kg/day)	3.1 ± 1.1	5.0 ± 2.0	**0.001**
Fat			
Mean ± SD (g/kg/day)	0.9 ± 0.3	1.3 ± 0.3	**0.001**
Type of ILE			
20% Clinoleic	6 (33.3%)	8 (30.8%)	0.858
20% SMOF lipid	12 (66.7%)	18 (69.2%)	
Infection			
No	16 (88.9%)	13 (50.0%)	**0.006**
Yes	2 (11.1%)	13 (50.0%)	

p-value < 0.05 indicates statistical significance.
Abbreviations: PNALD, parenteral nutrition-associated liver disease; SGA, subjective global assessment; SD, standard deviation; ILE, intravenous lipid emulsion.

day and ≥1 g/kg/day, according to the result from the difference of mean fat between two groups (Table 3). Simple logistic regression of new categorical fat variable was also significantly different with an odds ratio of 6.6 (95% CI: 1.69–25.71; $p = 0.007$) and the VIF method showed no multicollinearity with other risk factors. Consequently, multiple logistic regression analysis was done by including all significant risk factors from the simple method. Interestingly, only severe malnutrition by SGA and the amount of carbohydrate were independent risk factors for PNALD with an odds ratio of 13.25 (95% CI: 1.37–128.24; $p = 0.026$) and 21.61 (95% CI: 1.81–258.56; $p = 0.015$), respectively (Table 4).

4. Discussion

In this study, we investigated the incidence and risk factors of PNALD in hospitalized adults receiving PN. The incidences of PNALD in previous studies varied from 25% to 100% [1,2]. This can be explained by the differences in the study population and different definitions of PNALD used for each study. The incidence of PNALD in our study was 59.1%. The incidence from our study corroborated the incidence of PNALD (57%) from a previous study which was conducted in the same group of patients [8]. Despite the changes of PN formulation and PN recommendation, the incidence of PNALD remains unchanged.

From the previous reports, the most common early manifestation of PNALD during the first 1–3 weeks after PN infusion was steatosis, while cholestasis rarely occurred during this period [3,14]. In a previous study, 27.5% of patients had steatosis and 15% had cholestasis [8]. Interestingly, our study found an opposite result; the incidence of cholestasis was higher than steatosis by 11.4% (34.1% vs. 22.7%). Hepatitis is believed to be the manifestation of steatosis that may result from overfeeding of energy, carbohydrate, or fat [1,12,15]. This discrepancy may be due to the lower estimated macronutrient requirements for PN, compared with the practice 10 or more years ago [12] On the other hand, the increase of the proportion of cholestasis might be partly due to CRBSI, which is an important risk factor of PNALD [16]. It can be seen that there was a higher incidence of CRBSI in the cholestasis group than the steatosis group (20% vs. 10%, $p = 0.596$). However, the statistical insignificance may cause from underpower of the study. Mixed steatosis and cholestasis rarely occurred in the early phase of PN. The most common imaging finding in early phase of PNALD was unremarkable. Imaging finding of fatty liver rarely showed up in PNALD (1 patient in the steatosis group and 1 patient in the mixed group). In our study, there was no cholecystitis, gallstones, or gallbladder sludge from the abdominal ultrasound.

The time course of PNALD in this study was consistent with previous reports; PNALD usually occurred within 1–4 weeks after PN initiation [1]. The median onset of PNALD in our study was 12.5 days (range: 4–42 days). Nevertheless, we found that the onset of steatosis was the same as cholestasis with median onset of 13 days and 12 days, respectively. From this finding, cholestasis was not necessarily the late manifestation as proposed in the previous reports and could occur as early as 6 days post PN treatment [17]. Additionally, the mild severity of abnormal liver tests, with minimal elevation of only 1.7 to 2.2 times, also supported the results from previous reports [8,12,18].

Previous studies described several key factors that affected the occurrence of PNALD. These included patient-related causes such as sepsis, poor oral intake, and bacterial overgrowth, and PN-related

Table 4
Odds ratio of risk factors for parenteral nutrition-related liver disease.

Factors	Simple Logistic Regression Analysis			Multiple Logistic Regression Analysis		
	Odd ratio	95% CI	*p*-value	Odd ratio	95% CI	*p*-value
Nutrition status						
SGA B	1	–	–	1	–	–
SGA C	8.40	2.11–33.48	**0.003**	13.25	1.37–128.24	**0.026**
Energy (kcal/kg/day)	1.11	1.02–1.20	**0.013**	0.82	0.64–1.04	0.104
Carbohydrate (g/kg/day)	4.21	1.79–9.89	**0.001**	21.61	1.81–258.56	**0.015**
Carbohydrate						
<4 g/kg/day	1	–	–			
≥4 g/kg/day	19.25	4.13–89.74	**<0.001**			
Fat (g/kg/day)	178.30	7.42–4282.8	**0.001**			
Fat						
<1 g/kg/day	1	–	–	1	–	–
≥1 g/kg/day	6.60	1.69–25.71	**0.007**	0.51	0.02–11.20	0.666
Type of ILE						
20%Clinoleic	1	–	–			
20%SMOF lipid	1.12	0.31–4.07	0.858			
Infection						
No	1	–	–	1	–	–
Yes	8	1.52–42.02	**0.014**	7.23	0.48–107.93	0.152

p-value<0.05 indicates statistical significance.
Abbreviations: CI, confidence interval; SGA, subjective global assessment; ILE, intravenous lipid emulsion.

causes such as calorie excess, fat excess, carbohydrate excess, types of ILE, phytosterols, and nutrient deficiencies [1–3,19]. Our study also revealed the associations between PNALD and several risk factors in simple logistic regression analysis, including severe malnutrition by SGA C, higher energy intake, higher carbohydrate and fat intake, and presence of infection. However, the types of ILE in our study showed no significant association with PNALD. The role of fat source in PNALD involves high concentration of omega-6 fatty acid and significant amount of phytosterols. The omega-6 fatty acid potentially can initiate or worsen inflammation because it can be metabolized into proinflammatory eicosanoids such as prostaglandins and leukotrienes [20]. In addition, phytosterols are ineffectively metabolized to bile acids, resulting in poor bile flow, and can cause cholestasis, biliary stones and sludge [21]. The high proinflammatory omega-6 concentration and phytosterols may cause liver injuries in patients receiving PN with soybean oil-based ILE [22]. The negative association between types of ILE and PNALD in this study may be due to the use of newer ILE in our hospital. These types of ILE (20% SMOF® lipid, omega-6 fatty acid 2.85 g/100 mL and phytosterol 179–207 mg/L, and 20% Clinoleic®, omega-6 fatty acid 1.4–2.2 g/100 mL and phytosterol 227–274 mg/L) had lower amounts of omega-6 fatty acid and phytosterols, compared to the soybean oil-based ILE (20% Intralipid®, omega-6 fatty acid 5 g/100 mL and phytosterol 315–381 mg/L). The incidence of PNALD was not significantly different between patients receiving 20% Clinoleic® and SMOF® lipid. The potential anti-inflammatory effect of fish oil [23] found in SMOF® lipid may not be as important as omega-6 fatty acid and phytosterols found in ILE.

Nevertheless, in multiple logistic analysis, only severe malnutrition by SGA C and the amount of carbohydrate were independent risk factors for PNALD with an odds ratio of 13.25 (95% CI: 1.37–128.24; $p = 0.026$) and 21.61 (95% CI: 1.81–258.56; $p = 0.015$), respectively. Severe malnutrition has never been reported as a risk factor for PNALD. Malnourished patients have a higher risk of nutrient deficiencies which may be one of the possible causes of PNALD. One example is that essential fatty acid deficiency (EFAD) can lead to impaired lipoprotein formation and triglyceride secretion from the liver resulting in liver steatosis [12]. Carnitine and choline also play an important role in lipid metabolism. Therefore, deficiencies of these nutrients may lead to PNALD. Carnitine and choline deficiencies were previously believed to be the result of inadequacy in PN solution; however, severe malnutrition itself may contribute to subclinical deficiencies of nutrients and cause liver injuries after receiving PN [24]. Additional studies are needed to ascertain the roles of carnitine and choline as supplements for severely malnourished patients before receiving PN. Moreover, immune function may be impaired in severely malnourished patients which can result in infection and liver injuries.

Excess carbohydrates were the only significant independent PN-related risk factor in our study. Excess carbohydrates stimulate insulin release and inhibit mitochondrial fatty acid oxidation resulting in liver steatosis [19,25]. One study showed that liver steatosis occurred when glucose infusion rate was more than 5 mg/kg/min (7.2 g/kg/day) [15]. In our study, patients with PNALD had significant higher mean carbohydrate than patients without PNALD (3.1 vs. 5 g/kg/day, $p = 0.001$), and that the infusion of carbohydrate more than 4 g/kg/day was a risk factor for PNALD with an odds ratio of 19.25 (95% CI: 4.13–89.74; $p < 0.001$). Our finding emphasizes the importance of amount of carbohydrates rather than fat and total energy as the risk factor for PNALD, especially in hospitals that use newer types of ILE.

To the best of our knowledge and based on our review of the literature, this is the first study that showed severe malnutrition as an independent risk factor for PNALD. In our study, non-PN etiologies of liver injuries, including underlying liver diseases, viral hepatitis, drugs and toxins, ischemic hepatitis, and biliary diseases, were excluded in order to achieve the most accurate diagnosis of PNALD. However, this study also has some mentionable limitations. First, some causes of liver injuries such as infection are very difficult to exclude. Nevertheless, PNALD is recognized as liver dysfunction in patients receiving PN that results from a complex set of risk factors. Additionally, infection is considered as one of the risk factors for PNALD rather than a distinctive cause of liver diseases [2]. Second, liver biopsy was not done in this study because of its potential complications and no pathognomonic finding for the diagnosis of PNALD.

5. Conclusion

In conclusion, PNALD was very common and occurred in around two-thirds of the adults receiving PN in acute care setting. In contrast to previous studies, cholestasis was more common than steatosis, and the median onset was not different between each subtype. In severely malnourished patients, physicians need to exercise caution and monitor for PNALD, intensively. Excess amount of carbohydrate should be avoided and administration of carbohydrates less than 4 g/kg/day should be considered.

Statement of authorship

Narisorn Lakananurak contributed to the conception and design of the research. All authors contributed to the acquisition, analysis, and interpretation of the data. All authors drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Funding disclosure

None declared.

Conflicts of interest

None declared.

Acknowledgements

The authors gratefully acknowledge the Research Affair, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, for their helpful advices on statistical matters.

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