www.jpnim.com Open Access eISSN: 2281-0692
Journal of Pediatric and Neonatal Individualized Medicine 2026;15(1):e150116
doi: 10.7363/150116
Received: 2025 Aug 07; revised: 2025 Sept 08; accepted: 2025 Sept 21; published online: 2026 Apr 30

Original article

Triglyceride response to intravenous lipid emulsion in small vs non-small for gestational age newborns: a retrospective cohort

Sagee Nissimov[1,2], Lilach Hofi[3], Sharon Sarah Cahanovitc[3], Yael Simpson-Lavy[3], Dotan Shaniv[3,4], Calanit Hershkovich-Shporen[3,5]

[1]Department of Neonatology, Shamir Medical Center, Zerifin, Israel
[2]Gray Faculty of Medical & Health Sciences, Tel-Aviv University, Tel-Aviv, Israel
[3]Department of Neonatology, Kaplan Medical Center, Rehovot, Israel
[4]Pharmacy Services, Kaplan Medical Center, Rehovot, Israel
[5]Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel

Abstract

Background: Small for gestational age (SGA) infants may have reduced lipid tolerance during intravenous lipid emulsion (ILE) therapy. We compared triglyceride (TG) levels in SGA versus non-SGA neonates receiving ILE and explored associations with neonatal morbidities.

Methods: This retrospective study included neonates who received ILE for at least 24 hours. TG levels were measured at approximately 24 hours of life and at 30-60 days. Statistical analyses compared TG levels, the incidence of hypertriglyceridemia (TG > 250 mg/dL), and the change in TG levels over time between the groups.

Results: 165 neonates were included, 56 (33.9%) SGA and 109 (66.1%) non-SGA. The mean ± SD gestational age at birth and birth weight were 34.2 ± 3.0 vs. 29.8 ± 2.6 weeks ($p < 0.001$), and 1,446 ± 336 vs. 1,325 ±

350 grams, respectively (p = 0.02). TG levels at 24 hours were significantly higher in the SGA group (144 [98, 189] vs. 85 [62, 116] mg/dL, p < 0.001). Incidence of hypertriglyceridemia was higher in SGA infants (10.7% vs. 1.8%, p = 0.019). Despite shorter duration of exposure (3.0 [2.0, 4.5] vs. 4.5 [3.0, 7.0] days, p < 0.001), a subgroup of SGA infants with follow-up data had higher TG levels at 30-60 days of life compared to non-SGA infants (106 [84, 155] vs. 70 [56, 91] mg/dL, p = 0.005). In multivariable analysis, SGA status, intraventricular hemorrhage, use of cardiotropic agents, and ClinOleic (vs. SMOFlipid) were independently associated with higher TG at 24 hours.

Conclusion: SGA infants showed higher early TG levels and greater risk of hypertriglyceridemia during ILE, with elevations persisting at 30-60 days in the subgroup of SGA infants with follow-up data available. These findings support early TG monitoring and individualized lipid titration for SGA infants. Interpretation should consider the retrospective single-center design, baseline differences between SGA and non-SGA infants, and limited SGA follow-up sampling.

Keywords

Small for gestational age, intravenous lipid emulsion, hypertriglyceridemia, neonatal nutrition, metabolic response.

Corresponding author

Sagee Nissimov, Department of Neonatology, Shamir Medical Center, Zerifin, Israel; ORCID 0000-0001-7873-5224; tel.: 972 89779080; email: sageen@shamir.gov.il.

How to cite

Nissimov S, Hofi L, Cahanovitc SS, Simpson-Lavy Y, Shaniv D, Hershkovich-Shporen C. Triglyceride response to intravenous lipid emulsion in small vs non-small for gestational age newborns: a retrospective cohort. J Pediatr Neonat Individual Med. 2026;15(1):e150116. doi: 10.7363/150116.

Introduction

The use of intravenous lipid emulsions (ILEs) is widely recommended in neonatal care as they provide essential fatty acids, and non-protein calories critical for supporting growth and development in preterm and critically ill neonates [1, 2]. The current consensus is to commence ILE administration soon after birth at a relatively low dose and gradually increase it in accordance with the nutritional requirements of the patient while monitoring triglyceride (TG) levels to avoid hypertriglyceridemia [3, 4]. However, despite the fact that ILE are a mainstay of parenteral nutrition in neonates, several aspects of their use remain insufficiently explored. Notably, there is limited data regarding the tolerance and metabolic handling of ILE in small for gestational age (SGA) infants compared to non-SGA infants. The former are thought to be particularly vulnerable to ILE-associated adverse effects due to immature metabolic pathways, including reduced activity of lipoprotein lipase and other enzymatic systems involved in lipid metabolism [5, 6]. Given the scarcity of data, specific recommendations for ILE administration for this population are still absent. This retrospective cohort study aimed to compare serum TG levels in SGA and non-SGA neonates receiving ILE at two time points: 24 hours of life and 30-60 days.

Methods

Study design and settings

This single-center retrospective cohort study was conducted at the Neonatal Intensive Care Unit (NICU) of Kaplan Medical Center, a tertiary care hospital in Israel. The study population included neonates admitted to the NICU between April 2015 and December 2019 who received ILE as part of their parenteral nutrition regimen. According to the internal NICU guideline, ILE are promptly initiated for all infants with a birth weight below 1,800 grams. The typical initial dose is 2 grams per kilogram per day (g/kg/d), with dose escalation of an additional 0.5 g/kg/d every 24 hours as appropriate to a maximum of 3 g/kg/d. The protocol recommends serum TG sampling at 24 hours of life, while follow-up levels are obtained at the discretion of the attending physician. Hypertriglyceridemia, defined as TG levels exceeding 250 milligrams per deciliter (mg/dL) [7], typically prompts a reduction of ILE dose to 1 g/kg/d, whereas TG levels > 300 mg/dL necessitate discontinuation of ILE for at least 24 hours, with re-introduction of ILE pending repeat TG level assessment. During the study period the choice and availability of ILE transitioned gradually from ClinOleic (Baxter

Healthcare Ltd., United Kingdom) to SMOFlipid (Fresenius Kabi, Uppsala, Sweden). Omegaven (Fresenius Kabi, Graz, Austria) was provided as second-line ILE in cases of cholestasis. Enteral feeds are typically initiated within 6-24 hours of life, depending on the infant's clinical stability. For infants with hemodynamic instability, enteral feeds were delayed for up to 48 hours. The initial feeding volume is usually 10-20 milliliter/kilogram/day (mL/kg/d), with subsequent increases of 20-35 mL/kg/d. At the time of the study, the Israeli donor milk bank had not yet been established, so infants included in this study were fed with either infant formula or mother's own milk. Enteral feeds were administered via gavage every 3 hours. SGA was defined as a birth weight below the 10th percentile for gestational age (GA) based on the Fenton growth charts. Non-SGA was defined as a birth weight at or above the 10th percentile for GA according to the same Fenton growth charts [8], and therefore, included both appropriate for gestational age (AGA) and large for gestational age (LGA) infants. The study was approved by Kaplan Medical Center Research Ethics Board in accordance with the Declaration of Helsinki (0181-19kmc). Due to its retrospective nature, informed consent was waived.

Study population

Eligible were infants who met the following criteria: i. received ILE for at least 24 hours during their NICU stay; ii. had documented serum TG levels at approximately 24 hours of life. Infants with major congenital anomalies, chromosomal abnormalities, incomplete medical records, and infants who died during the first 72 hours of life were excluded.

Study outcomes

The primary outcome was: TG levels at 24 hours of life. The secondary outcomes were: i. TG levels at 30-60 days of life; ii. incidence of hypertriglyceridemia defined as TG > 250 mg/dL; iii. the change in TG levels between 24 hours of life and 30-60 days of life.

Data collection

Demographic and perinatal characteristics of infants were extracted from the NICU electronic database – Metavision (IMD-Soft®) – and included GA at birth, birth weight, and SGA/non-SGA status, the type and duration of ILE exposure; other medications received such as antibiotics, blood products, inotropic or vasopressor support and caffeine were extracted, as well.

Outcome data included TG levels at 24 hour of life, and at 30-60 days of life, as well as prematurity-related morbidities such as respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD) defined as need for oxygen or any type of respiratory support at 36 weeks post-menstrual age [9], patent ductus arteriosus (PDA) defined as a moderate-large duct, early-onset sepsis (EOS) defined as a positive blood culture taken within the first 72 hours of life, late-onset sepsis (LOS) defined as a positive blood culture taken after the first 72 hours of life, necrotizing enterocolitis (NEC) diagnosed according to the modified Bell's staging criteria if the stage was 2a or above [10], intraventricular hemorrhage (IVH) diagnosed by ultrasound examination and graded according to Papile's classification [11], and periventricular leukomalacia (PVL) diagnosed by the presence of multiple periventricular cysts identified by cranial ultrasound examination performed after 28 days of life.

Statistical analysis

Data were compiled into electronic spreadsheets and analyzed using SPSS® software (version 25.0; IBM Corp., Armonk, NY). Continuous variables were presented as means and standard deviations or medians and interquartile ranges (IQRs), depending on data distribution. Categorical variables were expressed as frequencies and percentages. Given the non-normal distribution of the data, non-parametric tests were employed: the Mann-Whitney U test was used to compare differences between independent groups, and the Related-Samples Wilcoxon Signed Rank Test was used for paired comparisons. Associations between categorical variables were assessed using Pearson's Chi-square test. Statistical significance was defined as a p-value < 0.05.

Additionally, a multiple linear regression analysis was performed to examine the relationship between log-transformed TG levels at 24 hours and a set of independent variables, including SGA vs. non-SGA diagnosis, gender, GA at birth, IVH, antibiotic treatment, cardiotropic support, and

type of ILE used (ClinOleic vs. SMOFlipid). First, a full model was built incorporating all predictors to assess their joint contribution to the variance in TG levels. Subsequently, a stepwise selection procedure was applied using Akaike Information Criterion (AIC) to identify the optimal model, aiming to balance model fit and simplicity. The step AIC function was utilized, allowing both forward and backward selection (direction = "both"), with the goal of excluding non-significant predictors and avoiding overfitting. The final model (best model) was chosen based on the lowest AIC. The percentage change in TG levels for each predictor was calculated using the formula $\%Change = (e\beta - 1) \times 100$.

Results

A total of 165 neonates were included in the analysis (**Fig. 1**); 56 (33.9%) in the SGA group and 109 (66.1%) in the non-SGA group. The mean ± SD GA at birth, and birth weight for the SGA and non-SGA groups were 34.2 ± 3.0 vs. 29.8 ± 2.6 weeks ($p < 0.001$), and 1,446 ± 336 vs. 1,325 ± 350 grams, respectively ($p = 0.02$), as presented in **Tab. 1**.

The ILE administered during the study period were SMOFlipid (69%), ClinOleic (19%), a combination of both (10%), and Omegaven (in combination with either SMOFlipid or ClinOleic) (2%). Exposure to SMOFlipid was more common in the non-SGA group than in the SGA group (75% vs. 57%, $p = 0.003$), while exposure to ClinOleic was higher in the SGA group (32% vs. 12%, $p = 0.003$) (**Tab. 1**). The median (IQR) duration of exposure to ILEs in the SGA and non-SGA groups were 3.0 (2.0, 4.5), and 4.5 (3.0, 7.0) days, respectively ($p < 0.001$), as presented in **Tab. 2**.

The median (IQR) TG levels at 24 hours of life were significantly higher in the SGA group compared to the non-SGA group (144 [98, 189] vs. 85 [62, 116] mg/dL, $p < 0.001$). Among the SGA group, birth weight Z-score was -2.18 ± 0.68, and was inversely, though not significantly,

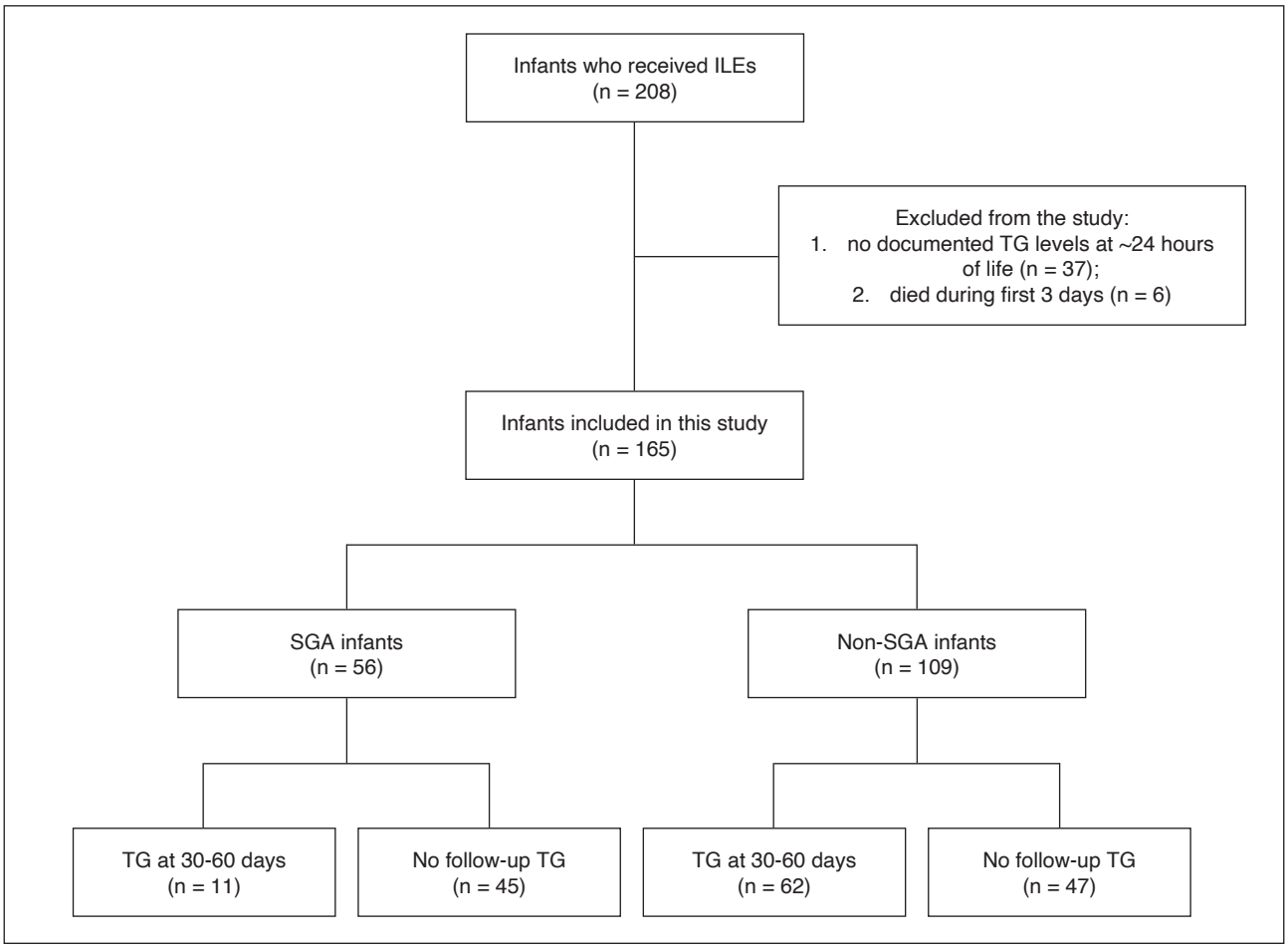

Figure 1. Study flowchart for patients included in the analysis comparing triglyceride (TG) levels of small for gestational age (SGA) and non-SGA infants.
ILEs: intravenous lipid emulsions; SGA: small for gestational age; TG: triglycerides.

Table 1. Comparison of demographics, prematurity-related outcomes and intravenous lipid emulsions (ILEs) administered between small for gestational age (SGA) and non-SGA infants who received ILE for at least 24 hours.

Characteristic		SGA group (n = 56)	Non-SGA group (n = 109)	p-value
GA at birth (weeks)		34.2 ± 3.0	29.8 ± 2.6	**< 0.001**
Birth weight (grams)		1,446 ± 336	1,325 ± 350	**0.02**
Male sex		24 (43%)	58 (53%)	0.2
RDS		7 (13%)	58 (53%)	**< 0.001**
BPD		4 (7.1%)	33 (30%)	**< 0.001**
PDA		5 (8.9%)	38 (35%)	**< 0.001**
EOS		1 (1.8%)	3 (2.8%)	> 0.9
LOS		2 (3.6%)	9 (8.3%)	0.3
NEC		1 (1.8%)	6 (5.5%)	0.4
IVH		2 (3.6%)	16 (15%)	**0.03**
PVL		0 (0%)	2 (1.8%)	0.5
Antibiotic treatment		26 (46%)	101 (93%)	**< 0.001**
Cardiotropic support		4 (7.1%)	11 (10%)	0.5
Administration of blood products		12 (21%)	30 (28%)	0.4
Caffeine treatment		12 (21%)	95 (87%)	**< 0.001**
ILEs	SMOFlipid	32 (57%)	82 (75%)	**0.003**
	ClinOleic	18 (32%)	13 (12%)	
	SMOFlipid and ClinOleic	4 (7%)	13 (12%)	
	SMOFlipid and Omegaven	2 (3.6%)	0 (0%)	
	ClinOleic and Omegaven	0 (0%)	1 (0.9%)	

Data are presented as number (frequency) or mean ± standard deviation, as appropriate.
BPD: bronchopulmonary dysplasia; EOS: early-onset sepsis; GA: gestational age; ILEs: intravenous lipid emulsions; IVH: intraventricular hemorrhage; LOS: late-onset sepsis; NEC: necrotizing enterocolitis; PDA: patent ductus arteriosus; PVL: periventricular leukomalacia; RDS: respiratory distress syndrome; SGA: small for gestational age.

related to TG levels at 24 hours (Pearson r = -0.151; 95% CI: -0.398, 0.116; p = 0.266) (**Fig. 2**).

Six infants (10.7%) in the SGA group had hypertriglyceridemia at 24 hours of life compared to 2 infant (1.8%) in the non-SGA group (p = 0.019). Follow-up TG levels at 30-60 days of life were available for 73 infants; 11 (15.1%) in the SGA group and 62 (84.9%) in the non-SGA group. In this subgroup, TG levels remained significantly higher in the SGA group compared to the non-SGA group (106 [84, 155] vs. 70 [56, 91] mg/dL, p = 0.005) (**Tab. 2**).

The non-SGA group experienced significantly more prematurity-related morbidities as well as higher rates of antibiotic and caffeine exposure (**Tab. 1**).

Among infants diagnosed with IVH (n = 18), compared to infants with no IVH (n = 147), TG levels at 24 hours were significantly higher (116 [86, 204] vs. 98 [68, 141] mg/dL, p = 0.019) (**Tab. 2**).

TG levels were also compared between infants who received SMOFlipid (n = 114) and infants who received ClinOleic (n = 31) as a sole ILE. For infants who received ClinOleic, TG levels at 24 hours were significantly higher than for those who received SMOFlipid (145 [111, 174] vs. 86 [68, 126] mg/dL, p < 0.001) (**Tab. 2**).

A multivariable linear regression on log-transformed TG at 24 hours found that being born SGA, the presence of IVH, the administration of cardiotropic agent, and the type of ILE used were independent risk factors for higher TG levels (**Tab. 3**).

Table 2. Triglyceride (TG) levels, intravenous lipid emulsion (ILE) administration, and their association with small for gestational age (SGA) status and intraventricular hemorrhage (IVH).

Characteristic	SGA group (n = 56)	Non-SGA group (n = 109)	p-value
TG levels at 24 hours of life (mg/dL)	144 (98, 189)	85 (62, 116)	**< 0.001**
Hypertriglyceridemia [a]	6 (10.7%)	2 (1.8%)	**0.019**
Duration of ILE administration (days)	3.0 (2.0, 4.5)	4.5 (3.0, 7.0)	**< 0.001**
TG levels at 30-60 days of life (mg/dL) [b]	106 (84, 155)	70 (56, 91)	**0.005**
Characteristic	**Group with no IVH (n = 147)**	**Group with IVH (n = 18)**	**p-value**
TG levels at 24 hours of life (mg/dL)	98 (68, 141)	116 (86, 204)	**0.019**
Characteristic	**Group who received SMOFlipid (n = 114)**	**Group who received ClinOleic (n = 31)**	**p-value**
TG levels at 24 hours of life (mg/dL)	86 (68, 126)	145 (111, 174)	**< 0.001**

Data are presented as number (frequency) or median (IQR), as appropriate.
ILE: intravenous lipid emulsions; IVH: intraventricular hemorrhage; mg/dL, milligram per deciliter; SGA: small for gestational age; TG: triglycerides.
[a] Hypertriglyceridemia was defined as TG levels above 250 mg/dL; [b] the number of patients for this analysis was 73 (11 in the SGA group, and 62 in the non-SGA group).

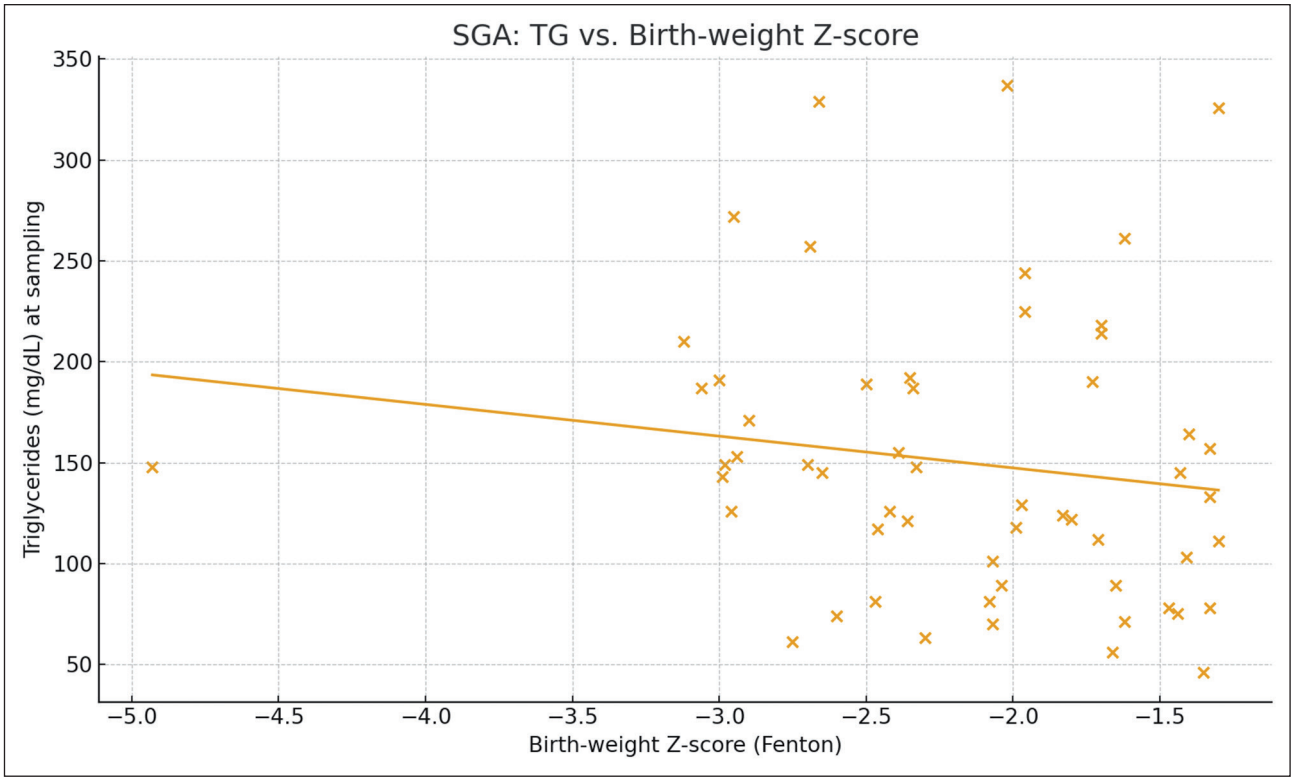

Figure 2. Scatter of triglycerides (TG) (mg/dL) vs. birth-weight Z-score among small for gestational age (SGA) infants with an overlaid linear fit.

Table 3. A multivariable linear regression analysis of factors associated with triglyceride (TG) levels.

	Full model				Best model				Percent of change	
	Estimate	Std. error	Statistic	p-value	Estimate	Std. error	Statistic	p-value	Full model	Best model
(Intercept)	1.808	0.219	8.276	**< 0.001**	1.887	0.02	95.653	**< 0.001**	-	-
SGA vs. non-SGA	0.172	0.042	4.133	**< 0.001**	0.181	0.031	5.772	**< 0.001**	18.77	19.84
Sex	0.004	0.029	0.125	0.901	-	-	-	-	0.40	-
GA at birth (weeks)	0.003	0.007	0.397	0.692	-	-	-	-	0.30	-
IVH	0.174	0.051	3.384	**0.001**	0.167	0.05	3.343	**0.001**	19.01	18.18
Antibiotic treatment	0	0.044	0.008	0.994	-	-	-	-	0.00	-
Cardiotropic support	0.124	0.059	2.085	**0.039**	0.114	0.053	2.128	**0.035**	13.20	12.08
ClinOleic vs. SMOFlipid	0.139	0.041	3.389	**0.001**	0.148	0.038	3.915	**< 0.001**	14.91	15.95
Other ILE vs. SMOFlipid	-0.029	0.046	-0.621	0.535	-	-	-	-	-2.86	-
Sample size	165				165				-	
R-squared	0.322				0.32					
Adjusted R-squared	0.287				0.303					

The dependent variable in the regression is a log-transformed value of triglyceride (TG) levels at 24 hours, as the original values were not normally distributed. The included variables were those that showed a significant association with TG levels at 24 hours, except for gender, that was included as a covariate.
GA: gestational age; ILE: intravenous lipid emulsion; IVH: intraventricular hemorrhage; SGA: small for gestational age.
R-squared and adjusted R-squared values indicate the proportion of variance explained by the model.

Discussion

In this retrospective study, we evaluated serum TG levels in SGA and non-SGA infants receiving ILE. Our findings suggest that SGA infants had significantly higher TG levels at 24 hours, as well as a higher incidence of hypertriglyceridemia. Among a limited subgroup of infants with available follow-up sampling at 30-60 days, TG levels remained higher in SGA infants. This

observation is consistent with previous studies highlighting the metabolic vulnerabilities of SGA infants, which may predispose them to hypertriglyceridemia [12, 13].

ILEs are a crucial component of the preterm infant's diet. As such, several guidelines exist to guide clinicians and dictate treatment, including one published by the American Society for Parenteral and Enteral Nutrition (ASPEN) [14], and one by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) [15]. Nevertheless, administration of ILEs is not devoid of adverse effects and may lead to hypertriglyceridemia, a condition associated with increased incidence of mortality [16], pulmonary hypertension [17], acute respiratory deterioration [18], and severe retinopathy of prematurity [16]. While the ASPEN and ESPGHAN guidelines specify the recommended initial dose and gradual increase of ILEs, they do not specifically address SGA infants, a population thought to be susceptible to hypertriglyceridemia [19, 20].

The elevated TG levels in SGA infants seen in our study are supported by the findings of Rabinowicz et al., who compared the incidence of hypertriglyceridemia in SGA infants born < 34 weeks GA to AGA infants who were matched for GA at birth, and found a significantly higher incidence of hypertriglyceridemia and higher TG levels in SGA infants [12]. While in that study the ILE used was ClinOleic, most infants in our study received SMOFlipid, a more commonly used ILE that offers additional beneficial effects and thus is more relevant to modern day NICUs [21, 22]. Also, TG levels in that study were drawn on the fourth day of life, whereas in our study the levels of TG were determined at 24 hours of life. While the incidence of hypertriglyceridemia in SGA infants in the previous study was 22.5%, we have witnessed a lower incidence of ~10%. This difference may be explained by the earlier sampling and, therefore, lower cumulative dosage administered in our study. Nevertheless, the fact that, in the previous study, higher levels were witnessed within a longer timeframe indicates that it may be prudent to apply early screening to allow adjustment of ILE dosage, which may in turn help to avoid hypertriglyceridemia and its adverse effects.

Exploratory analyses within the SGA group suggested that more severe growth restriction may be associated with higher early TG levels, consistent with biologic plausibility that impaired fetal growth could reflect altered postnatal lipid handling. However, in our dataset the correlations were modest and did not achieve statistical significance.

To the best of our knowledge, this study provides the first longitudinal monitoring of TG levels in SGA infants. A second measurement of TG levels during the second month of life was analyzed to assess whether the elevated TG levels persisted beyond the immediate neonatal period. We found that the elevated TG levels in SGA compared to non-SGA infants persisted when follow-up levels were taken at 30-60 days of life, despite a shorter duration of exposure in the SGA group. This finding may be explained by an impaired lipid metabolism in SGA infants. Several different mechanisms have been suggested as possible explanations, most notably: i. a reduced lipoprotein lipase activity which leads to slower clearance of TG from the plasma [5]; ii. a lower capacity to metabolize very-low-density lipoproteins [23]; iii. higher insulin concentrations and insulin-to-glucose ratios, which can affect lipid metabolism and contribute to elevated TG levels [24]; iv. a different metabolic profile – including higher levels of free fatty acids and reduced beta-oxidation rates – which contributes to the accumulation of TG in the plasma [25]. Although the implications of elevated TG levels remain unclear, these findings support a more cautious clinical approach in this population, as TG elevation may persist longer than expected.

An analysis of all infants who had IVH has shown that TG levels are higher in this population than in infants without IVH. Similarly, in a large retrospective study, Giretti et al. have shown that lipid tolerance, calculated as the ratio between administered ILE and TG levels, was negatively associated with several prematurity-related morbidities, including IVH [13]. The association between TG levels and the presence of IVH is likely due to the high levels of TG being a marker of disease severity and metabolic disturbances rather than the cause of it. However, high levels of TG may theoretically contribute to the formation of IVH through oxidative stress that impairs vascular integrity [26, 27], impaired hemorheology that can alter blood viscosity and therefore affect microcirculatory flow [28], vasoconstriction that may reduce cerebral blood flow [28], and by triggering an inflammatory

response that may exacerbate the fragility of the vessels in the germinal matrix [27].

The findings of our study should be interpreted in the context of some important limitations. Due to the retrospective nature of this study, some data including several antenatal and perinatal parameters were inconsistently documented and are therefore not reported in this study. In this retrospective dataset, maternal diabetes and other details needed to distinguish constitutional from diabetes-related LGA were inconsistently charted. As some LGA infants, particularly those of diabetic mothers, may have impaired metabolic profiles, this heterogeneity could introduce residual confounding. Within the SGA cohort, we could not reliably distinguish infants with intrauterine growth restriction (placental insufficiency) from constitutionally small infants due to inconsistent antenatal/perinatal data, and this phenotypic heterogeneity may entail differential lipid tolerance that could influence the observed associations. Although ILE initiation and escalation followed a standardized unit protocol, longitudinal parenteral lipid doses (g/kg/d) and enteral lipid intake were not captured in a uniform, extractable format; consequently, dose-normalized or dose-response analyses were not feasible. Additionally, TG levels at 30-60 days of life were only available for a subset of patients (n = 73, 11 in the SGA group, and 62 in the non-SGA group), which may introduce selection bias and negatively impact the generalizability of our findings. Also, by comparing SGA infants to non-SGA infants without matching of GA at birth, our groups were inherently different in terms of their level of prematurity. Therefore, comparison of prematurity-related morbidities is inadequate. However, we opted for this specific design in order to assess all SGA infants exposed to ILE other than just preterm infants, as this population was shown to be susceptible to hypertriglyceridemia regardless of prematurity [25]. Furthermore, as this study shows a significantly higher TG levels and a higher incidence of hypertriglyceridemia in SGA infants compared to a younger group with significantly more prematurity-related morbidities, this comparison only serves to strengthen the correlation between being born SGA and an abnormal lipid metabolism. During the study period and in keeping with the published literature, our unit shifted from using mainly ClinOleic to SMOFlipid. While we did find a higher incidence of exposure to ClinOleic among SGA infants compared to non-SGA infants, and we have reported that infants exposed to ClinOleic had higher TG levels than those exposed to SMOFlipid, a linear regression analysis found SGA to be an independent risk factor for higher TG levels at 24 hours; thus, the differences in ILE exposure are unlikely to have significantly contributed to our findings. Finally, the relatively small sample size limits the statistical power and generalizability of our findings, particularly for subgroup analyses.

Conclusion

In this single-center retrospective cohort, SGA infants receiving ILE had higher early TG levels and a greater frequency of hypertriglyceridemia compared with non-SGA infants who also received ILE. In the subgroup of SGA infants with follow-up data available, elevations persisted at 30-60 days. In view of the limitations described, these findings should be interpreted cautiously. Even so, they support early TG surveillance and individualized lipid titration for SGA infants and may help pave the way for prospective studies to define tailored nutritional support for this population.

Highlights

- SGA infants show elevated TGs at 24 hours post lipid infusion.
- Higher hypertriglyceridemia incidence in SGA compared to non-SGA neonates.
- Persistently elevated TGs in SGA infants at 30-60 days of life.
- Early TG screening suggested for SGA infants on lipid emulsions.
- First longitudinal data on TG levels in SGA neonates post-ILE.

Declaration of interest

The Authors declare that they have no potential conflicts of interest that might be relevant to the contents of this manuscript. The Authors have no relevant financial interests to disclose. This research received no specific grant from any funding agency.

References

1. Chan AP, Rostas S, Rogers S, Martin CR, Calkins KL. Parenteral Nutrition in the Neonatal Intensive Care Unit: Intravenous Lipid Emulsions. Clin Perinatol. 2023;50:575-89.

2. ESPGHAN and ESPEN Guidelines Paediatric Parenteral Nutrition – Annex: List of Products. J Pediatr Gastroenterol Nutr. 2005;41:S85-7.
3. Frazer LC, Martin CR. Parenteral lipid emulsions in the preterm infant: current issues and controversies. Arch Dis Child Fetal Neonatal Ed. 2021;106:F676-81.
4. Frost B, Martin CR, Calkins KL. Dilemmas in the delivery of intravenous lipid emulsions and approach to hypertriglyceridemia in very preterm and low birth weight infants. J Perinatol. 2023;43:1189-93.
5. Fuwa K, Nagano N, Kitamura Y, Iwata F, Okada T, Morioka I. Umbilical cord blood stearoyl-CoA desaturase index and lipoprotein lipase mass level in small-for-gestational age newborns. Prostaglandins Leukot Essent Fatty Acids. 2020;156:102028.
6. Morillas J, Moltó L, Robles R, Gil A, Sánchez-Pozo A. Lipoprotein changes in small-for-gestational-age infants fed nucleotide-supplemented milk formula. Acta Paediatr. 1994;83:481-5.
7. Correani A, Giretti I, Antognoli L, Monachesi C, Cogo P, D'Ascenzo R, Biagetti C, Carnielli VP. Hypertriglyceridemia and Intravenous Lipid Titration During Routine Parenteral Nutrition in Small Preterm Infants. J Pediatr Gastroenterol Nutr. 2019;69:619-25.
8. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatr. 2013;13:1-13.
9. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med. 2001;163(7):1723-9.
10. Bell MJ, Ternberg JL, Feigin RD, Keating JP, Marshall R, Barton L, Brotherton T. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. Ann Surg. 1978;187:1-7.
11. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr. 1978;92:529-34.
12. Rabinowicz S, Levkovitz O, Leibovitch L, Schushan-Eisen I, Morag I, Rosen C, Maayan-Metzger A, Strauss T. Increased risk for early hypertriglyceridemia in small for gestational age preterm infants. Eur J Pediatr. 2020;179:1873-9.
13. Giretti I, D'Ascenzo R, Correani A, Antognoli L, Monachesi C, Biagetti C, Pompilio A, Marinelli L, Burattini I, Cogo P, Carnielli VP. Hypertriglyceridemia and lipid tolerance in preterm infants with a birth weight of less than 1250 g on routine parenteral nutrition. Clin Nutr. 2021;40:4444-8.
14. Cober MP, Gura KM, Mirtallo JM, Ayers P, Boullata J, Anderson CR, Plogsted S; ASPEN Parenteral Nutrition Safety Committee. ASPEN lipid injectable emulsion safety recommendations part 2: Neonate and pediatric considerations. Nutr Clin Pract. 2021;36(6):1106-125.
15. Lapillonne A, Fidler Mis N, Goulet O, van den Akker CHP, Wu J, Koletzko B; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids. Clin Nutr. 2018;37(6 Pt B):2324-36.
16. Sinclair R, Schindler T, Lui K, Bolisetty S. Hypertriglyceridaemia in extremely preterm infants receiving parenteral lipid emulsions. BMC Pediatr. 2018;18:1-7.
17. Prasertsom W, Phillipos EZ, Van Aerde JE, Robertson M. Pulmonary vascular resistance during lipid infusion in neonates. Arch Dis Child Fetal Neonatal Ed. 1996;74:F95-8.
18. Badr M, Goulard M, Theret B, Roubertie A, Badiou S, Pifre R, Bres V, Cambonie G. Fatal accidental lipid overdose with intravenous composite lipid emulsion in a premature newborn: a case report. BMC Pediatr. 2021;21:1-10.
19. Vlaardingerbroek H, Vermeulen MJ, Rook D, van den Akker CH, Dorst K, Wattimena JL, Vermes A, Schierbeek H, van Goudoever JB. Safety and efficacy of early parenteral lipid and high-dose amino acid administration to very low birth weight infants. J Pediatrics. 2013;163:638-644.e5.
20. Hossain MA, Islam MN, Shahidullah M, Akhter H. Serum triglyceride level in IUGR babies and its comparison with preterm AGA and term normal babies. Mymensingh Med J. 2006;15: 180-2.
21. Deshpande G, Simmer K, Deshmukh M, Mori TA, Croft KD, Kristensen J. Fish Oil (SMOFlipid) and Olive Oil Lipid (Clinoleic) in Very Preterm Neonates. J Pediatr Gastroenterol Nutr. 2014;58:177-82.
22. Huff KA, Nayak SP, Ahmad I, DiGeronimo R, Hair A, Kim JH, Markel T, Piazza A, Reber K, Roberts J, Sharma J, Sullivan K, Ahmad KA, Yanowitz T, Premkumar MH. Patterns of lipid-injectable emulsion use in neonatal intensive care units across the United States: A multi-institution survey. J Parenteral Enteral Nutr. 2023;47:51-8.
23. Morillas JM, Moltó L, Robles R, Gil A, Sánchez-Pozo A. Lipoproteins in preterm and small-for-gestational-age infants during the first week of life. Acta Paediatr. 1992;81: 774-8.
24. Wang X, Cui Y, Tong X, Ye H, Li S. Glucose and lipid metabolism in small-for-gestational-age infants at 72 hours of age. J Clin Endocrinol Metab. 2007;92:681-4.
25. Andrew G, Chan G, Schiff D. Lipid metabolism in the neonate: III. The ketogenic effect of Intralipid infusion in the neonate. J Pediatr. 1978;92:995-7.
26. Pitkäken OM. Peroxidation of lipid emulsions: a hazard for the premature infant receiving parenteral nutrition? Free Radic Biol Med. 1992;13:239-45.
27. Deshpande GC, Cai W. Use of Lipids in Neonates Requiring Parenteral Nutrition. JPEN J Parenter Enteral Nutr. 2020;44(Suppl 1): S45-54.
28. Kessler U, Zachariou Z, Raz D, Poeschl J, Linderkamp O. Effects of Intralipid infusion on hemorheology and peripheral resistance in neonates and children. Pediatr Surg Int. 2005;21: 197-202.