Scientific Research Publishing

Open Journal of Pediatrics, 2026, 16(6), 799-807
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Major Hypertriglyceridemia in Children: About Two Cases Revealed by Complications, at the Charles de Gaulle University Hospital Center (Ouagadougou)

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How to cite this paper:
Kabore/Ouedraogo, A., Kalga, D., Togueyeni/Tamini, L., Konate, B., Soudre, F., Zoungrana, C. and Ye/Ouattara, D. (2026) Major Hypertriglyceridemia in Children: About Two Cases Revealed by Complications, at the Charles de Gaulle University Hospital Center (Ouagadougou). *Open Journal of Pediatrics*, **16**, 799-807.
https://doi.org/10.4236/ojped.2026.166077

Received: September 21, 2026
Accepted: November 10, 2026
Published: November 13, 2026

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Abstract

Hypertriglyceridemia is relatively common in adults but rare in children. It is potentially serious due to its complications, the main ones being acute pancreatitis and stroke. We report the case of hypertriglyceridemia in a seventeen-day-old newborn and a 14-month-old infant respectively. The milky appearance of the blood had led to suspicion of lipids disorder, and the lipid profile confirmed hypertriglyceridemia. The course was fatal in the newborn. In the infant case, after starting medical treatment and nutritional treatment, she suffered a stroke due to a fat embolus. The outcome was favorable after motor rehabilitation sessions.

Keywords

Major Hypertriglyceridemia, Infant, Burkina Faso

1. Introduction

Hypertriglyceridemia is a dyslipidemia characterized by an increase in plasma triglycerides beyond 10 mmol/L (normal value 0.45 - 1.7 mmol/L) [1]. It can be isolated or mixed, linked to genetic factors [2] [3] or secondary to other pathologies [1].

Some studies in adolescents have shown relatively high frequencies. Thus, in the United States in 2020, this frequency was estimated at 1/1000 children accord-

ing to Patni *et al.* [4]; in France hypertriglyceridemia represented 12.3% of adolescent hospitalizations according to Maisonneuve *et al.* in 2009 [5]; in Tunisia, in 2014 Marrakchi *et al.* found 9.8% hypertriglyceridemia, still in adolescents [6].

In children, it is a rare pathology often reported in the form of isolated cases [7]-[9]. In children, it is often the familial or genetic form [1] occurring due to a severe deficiency of lipoprotein lipase, an enzyme that hydrolyzes triglycerides and chylomicrons into smaller particles.

In major hypertriglyceridemia, the accumulation of plasma triglycerides thus increases the risk of arteriosclerotic cardiovascular disease [10] [11] as well as the risk of acute pancreatitis [12].

2. Methodology

We report two cases of hypertriglyceridemia in a seventeen-day-old newborn and a 14-month-old infant respectively. This was a descriptive study of two cases received between December 2021 and April 2022 in the medical pediatrics department. The milky appearance of the blood had led to the suspicion of the lipid disorder and the lipid profile confirmed the hypertriglyceridemia.

3. Results

3.1. Observation 1

The newborn was admitted at 17 days of age for hypotonia.

As a history, the pregnancy uneventful following with five prenatal visits without complications and the birth occurred at term vaginally with a birth weight of 3250 g, a height of 50 cm and a head circumference of 35 cm. Apgar score were normal. Consanguinity was not reported and the mother had two other normal children. She had no known medical history and was not under treatment apart from iron and preventive antimalarial treatment antenatally.

On admission on 04/16/2021, the newborn had a poor general impression, impaired consciousness and skin and conjunctival pallor. The peripheral oxygen saturation was 87% in ambient air, a temperature of 38.5˚, a heart rate of 126 beats/minute, and a respiratory rate of 29 cycles/minute.

Physical examination also showed generalized hypotonia and blunted archaic reflexes. The diagnostic hypothesis of a late bacterial neonatal infection was suggested. At the intensive care unit, the newborn was put on oxygen and blood tests (hemogram, CRP, ionogram) were requested. Given the milky appearance of the blood during the sampling, a lipid profile was also carried out. These examinations were not performed while the newborn was fasting, as the newborn was in intensive care.

The results of the laboratory examinations were all disturbed. The laboratory infection profile showed leukocytes at 10,070/uL predominantly neutrophil at 7110/uL, lymphocytes at 1570/uL and monocytes at 1300/uL. The haemoglobin level at 19 g/dl, platelets at 50,000/uL, the CRP was at 282 mg/l, additionaly severe hyponatremis at 122 mmol/L was detecd.

Regarding the lipid profile, total cholesterol was 16.98 mmol/L (N = 3.5 - 5.2 mmol/L), triglycerides were 10.98 mmol/L (N = 0.45 - 1.7 mmol/L), LDL cholesterol was 10.51 mmol/L (N = 1.75 - 4.25 mmol/L) and HDL cholesterol was 4.53 mmol/L (N = 0.64 - 1.68 mmo/L). Casual blood glucose was very high at 61.8 mmol/L (N = 4.1 - 6.0 mmol/L).

The biologist notified the use of dilution techniques (1/10 or 1/100) during the biological examinations to obtain these results.

The newborn was then kept in intensive care, with essential care for newborns and was fed by breast milk through a nasogastric tube.

Process of his hospitalization is remarkable by the persistence of fever, by the onset of respiratory distress on the 4th day of hospitalization. Despite resuscitation measures, the newborn died on the seventh day of hospitalization in a picture of severe respiratory distress. Specific treatment of hypertriglyceridemia could not be started. Likewise, it was not possible to monitor the hypertriglyceridemia.

Figure 1 shows the milky appearance of the blood.

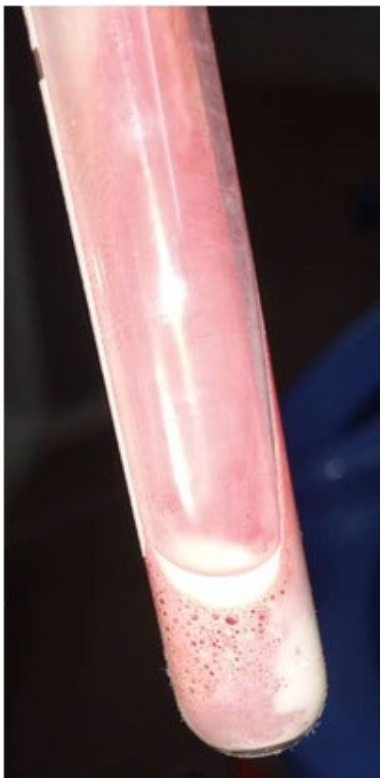


Figure 1. Image showing the milky appearance of blood from a dry tube sample in a 17-day-old newborn.

3.2. Observation 2

This is a 14-month-old female infant, referred to the medical emergency on 12/20/2021 by her attending physician for severe pallor.

Medical history revealed that the pregnancy was six prenatal consultations without complications and the birth occurred at term vaginally with a birth weight

of 3700 g, height of 51 cm. She would not have been resuscitated at birth. This infant had no medical history and was up to date with his vaccinations. The infant was in the process of weaning onto solid foods alongside breastfeeding.

Her mother was on her third pregnancy, she had three well developed children. She had no known medical history and was not under treatment apart from iron and preventive antimalarial treatment antenatally. Neither parent would have any follow-up for hypercholesterolemia.

On admission (at 14-month-old), the general condition was maintained, consciousness was normal, the weight was 7.45 kg and the height was 74 cm (weight/height ratio < −2 SD). The peripheral oxygen saturation was 97% in ambient air, the temperature at 37.3˚. The respiratory rate was 22 cycles/minute, the heart rate 130 beats/minute.

Physical examination noted a triangular face with a broad forehead, a large collateral venous circulation on the scalp and forehead. There was no fatty nodule on the skin. The examination of the appliances was otherwise normal apart from furunculosis in the right buttock.

Laboratory tests were carried out and in view of the milky appearance of the blood, the initial tests were completed by the lipid profile.

The infant was not fasting at the time of this initial sample collection. The laboratory tests were performed using the appropriate methods and techniques. A 1/20 dilution was performed, consisting of mixing 1 volume of serum with 19 volumes of distilled water (50 µL of serum + 950 µL of distilled water), to obtain a total of 20 volumes. Triglycerides were quantified using a colorimetric enzymatic method based on the hydrolysis of triglycerides by lipase, followed by enzymatic reactions involving glycerol kinase, glycerol phosphate oxidase, and peroxidase. The intensity of the resulting color is proportional to the triglyceride concentration.

The results of these tests were disturbed with hyperleukocytosis at 22,770/µL predominantly neutrophil (14,170/µL), normochromic normocytic anemia with a hemoglobin level of 4 g/dl and platelets at 283,000/µL.

The lipid profile found plasma triglycerides at 56.56 mmol/L (N = 0.45 - 1.7 mmol/L), cholesterol at 10 mmol/L (N = 3.5 - 5.2 mmol/L), HDL cholesterol at 0.25 mmol/L (N = 0.64 - 1.68 mmol/L); and Casual blood glucose at 21.3 mmol/L (N = 4.1 - 6.0 mmol/L).

The cardiac Doppler ultrasound was normal. The Doppler ultrasound of the veins of the head, on the other hand, showed atherosclerotic plaques in the large vessels. The ophthalmological examination found a lipid deposit (Kayser's ring) in the corneal.

Urine culture, blood culture and chest X-ray were ordered but did not reveal an infectious focus. Abdominal ultrasound returned normal.

The initial management consisted of resuscitation combining a transfusion of a red blood cell; the initiation of antibiotic therapy; nutritional management involving a diet free from any animal fats, using only vegetable oil in meals and

acetylsalicylic acid 100 mg, administered orally for one month.

One month later, medical follow up showed on the clinical level a persistence of the veins of the head, a healing of the boils.

Laboratory tests showed a persistence of lipid abnormalities and even an increase in triglycerides. The lipid profile found cholesterol at 26.6 mmol/L (N = 3.5 - 5.2 mmol/L), HDL cholesterol at 1.18 mmol/L (N = 0.64 - 1.68 mmol/L), LDL cholesterol at 1.85 mmol/L (N = 1.75 - 4.25 mmol/L), triglycerides at 79.55 mmol/L (N = 0.45 - 1.7 mmol/L) and Casual blood glucose at 21.6 mmol/L (N = 4.1 - 6.0 mmol/L).

Then the management consisted in the diet with vegetable oils; omega 3 fatty acids (in syrup) at a rate of 3 drops/day for a month; acetyl salicylic acid 100 mg/day for a month and cholestyramine a sachet of 4 g/day for a month.

After this second month of treatment, the clinical examination showed a regression of the venous circulation of the forehead. However, the sudden paresis of the right upper limb motivated a readmission. The cerebral CT scan performed showed a stroke by thrombosis of the sagittal sinus, a significant dilation of the cortical veins associated with adjacent cerebral softening.



Figure 2. Image showing the milky appearance of the blood in a 14-month-old infant.

Biologically, the lipid profile was markedly improved, with cholesterol at 12.94 mmol/L (N = 3.5 - 5.2 mmol/L), HDL cholesterol at 1.23 mmol/L (N = 0.64 - 1.68 mmol/L), LDL cholesterol at 6.03 mmol/L (N = 1.75 - 4.25 mmol/L); triglycerides at 15 mmol/L and Casual Blood Glucose at 4.83 mmol/L (N = 4.1 - 6.0 mmo/L).

Treatment was initiated in the intensive care unit. The short-term evolution was favorable, marked by a total improvement in symptoms and discharge from hospital on the 7th day. Outpatient motor physiotherapy allowed total recovery of the right hemiparesis.

To date, the patient is in good health with good psychomotor and height and weight growth. The lipid profile has completely normalized. **Figure 2** shows the milky appearance of the blood.

4. Discussion

4.1. Circumstances of Discovery

Hypertriglyceridemia is relatively rare in infants. In the first case, screening was not proposed for the parents. In the second case, although the parents did not sign a written document, they provided their consent for an etiological investigation into their infant's hypertriglyceridemia. They agreed to undergo lipid profile testing, which returned normal results for both the mother and the father. Due to a lack of necessary technical facilities, we were unable to investigate potential genetic factors in their infant.

In our study the lactescent appearance of the blood observed incidentally during blood sampling. This appearance is characteristic of type I and V hypertriglyceridemia of the Fredrickson and al. classification [13] and may exist even before the onset of clinical signs depending on Tremblay and al. as well as Aly *et al.* [9] [14].

Depending on the type of hypertriglyceridemia, the blood may also have a normal or opalescent appearance. A particular aspect of the blood requires a complete lipid assay to look for dyslipidemia, even in the absence of suggestive clinical signs.

4.2. Clinical Signs

In our series, the 17-day-old newborn presented pallor, neurological disorders followed by respiratory distress that led to death.

Also, the 14-month-old infant presented with pale skin and hypotonia on admission. This same symptomatology had been reported by Girard *et al.* in 2015 [15]. The atypical nature of these symptoms can lead to diagnostic errors [2]. On the other hand, the collateral venous circulation of the forehead found in the 2nd case was easily noticed and corresponds to the accumulation of chylomicrons in the blood vessels creating atheromatous plaques.

These plaques had relevant of the seriousness of the disease and they predispose to fatty emboli. While such vascular events caused by fat emboli have been described by some authors [16] [11], our case is not sufficiently documented (due to the absence of an MRI) to establish a link with the atheromatous plaques observed

during the Doppler ultrasound.

Other complications of hypertriglyceridemia would also be pancreatitis found by other authors [1] [10], manifested by recurrent abdominal pain. In our series, neither clinical signs nor abdominal ultrasound have suggested pancreatitis.

4.3. Paraclinical Signs

In our study, the biological infectious syndrome in infants would probably be related to furunculosis. The elevation of cholesterol associated with hypertriglyceridemia is described in mixed forms [1] [12].

However, this lipid profile, as well as other biological examinations, can be strongly disturbed. This is due to the accumulation of lipoproteins in the sample, disturbing analytical techniques based on absorbance measurement, such as turbidimetry methods [17] There is also a modification of the volume distribution in the sample with a decrease in plasma free water, in this case distorting the results of certain tests [18]. In the patients included in our study, a dilution had been made and indicated by the biologist. Among these additional examinations, hyperglycemia had been observed at (61.8 mmol/L and 21.6 mmol/L) respectively in both cases. Other cohort studies have found type II diabetes in adult hypertriglyceridemia [16] Given the inadequacy of the technical platform and the high cost, no molecular biology examination with an etiological aim (enzymatic assay) could be performed.

4.4. Medical Care

In severe forms with severe respiratory distress, such as in the newborn in our series, the therapeutic measure indicated is emergency plasmapheresis [1] [19]. The limited technical platform did not allow this management.

Transfusion exchange is an emergency therapeutic alternative when plasmapheresis is not feasible according to Valaiyapathi *et al.* [19]. This was not applied in the newborn case.

In infants, a diet based on low-triglyceride formula and family meals free of animal fats has been described by other authors [20] [21]. The diet based on triglyceride-depleted milk formula and a diet without animal fats has been described by other authors Ghoor *et al.* [20] [21]. Molecules such as fibrates, omega-3 fatty acids, statins that are used in the treatment of hypertriglyceridemia in adults are said to have limited efficacy in children according to the study by Valaiyapathi *et al.* [19].

The newborn exhibited signs of infection, which contributed to its early death. As for the infant, the onset of hemiparesis during the course of treatment was transient and did not hinder a favorable outcome.

5. Conclusions

Hypertriglyceridemia in children is a relatively rare but not exceptional disease. Its diagnosis and management in children remain challenging in our work con-

text. Clinical signs are often atypical [22]. It is therefore necessary to effectively manage comorbidities and to advocate for etiological investigations in cases of hypertriglyceridemia.

Approaching patient-specific treatment goals and preventing complications and comorbidities remains paramount to avoid mortality.

Author Contributions

Aissata KABORE/OUEDRAOGO: Conception and redaction; Dominque Kalga: litteracy review; Laure Togueyeni/Tamini: Manuscrit analysis; Barguissa Konaté: data collection; Fabienne Soudre: Laboratory tests; YE Diarra/Ouattara: Manuscrit validation.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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