Journal of Ophthalmology & Eye Care
Volume 7 | Issue 1
ISSN: 2639-9296

Review Article Open Access

Lipemia Retinalis: A Case Report and Comprehensive Review with Emphasis on Infantile Cases

Homayoun Nikkhah[1, 2, 3], **Narges Karrabi**[1, 2, 3, *]

[1]Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Torfeh Eye Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Department of Ophthalmology, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[*]**Corresponding Author:** Narges Karrabi, Ophthalmic Research Center, Boostan 9 St., Pasdaran Ave., Tehran 16666-94516, Iran, Tel.: 98 9122972799, E-mail: karrabi.narges@gmail.com

Citation: Homayoun Nikkhah, Narges Karrabi (2024) Lipemia Retinalis: A Case Report and Comprehensive Review with Emphasis on Infantile Cases, J Ophthalmol Eye Care 7(1): 103

Received Date: June 25, 2024 **Accepted Date:** July 25, 2024 **Published Date:** July 29, 2024

Abstract

Background: Lipemia retinalis (LR) is a rare pathology characterized by creamy white retinal vessels due to chylomicronemia. Here, we present a case report of LR in a 44-day neonate and provide a comprehensive review of the literature on this rare condition.

Materials and Methods: All articles indexed in Pubmed and Google scholar with term "Lipemia retinalis" in title were included to provide a comprehensive review about clinical aspects of LR then an analysis was conducted on all infantile and neonatal cases of LR reported in the literature. Data on clinical presentation, ophthalmic findings, laboratory investigations, and treatment strategies were extracted and analyzed.

Results: Our case report details the presentation of a 44-day-old boy with creamy white retinal vessels consistent with LR, which was identified during screening for retinopathy of prematurity (ROP). A literature review yielded a total of 44 reported cases of LR in infants and neonates, bringing the total number of cases to 45 including ours. In cases where gender was specified, 27 (60%) were female and 15 (33.3%) were male. The average age of infants diagnosed with LR was 10.11±10.68 weeks, and their average gestational age (GA) and birth weight (BW) were 37.43±4.41 weeks and 2535.48± 1086.27 grams, respectively. Type 1 hyperlipoproteinemia (76.4%) was identified as the most common underlying cause, with 21 cases (46.7%) attributed to lipoprotein lipase (LPL) deficiency. Vomiting or poor feeding were the most common symptoms prompting evaluation in 13 cases (36.1%). In 40% of cases, the stage of LR was specifically identified, with 4 cases classified as stage 2 and 14 cases classified as stage 3. Organomegaly was the most common associated manifestation of hypertriglyceridemia when combined with LR, seen in 51.1% of cases. The GA was significantly correlated with the presence of xanthoma and pancreatitis (p = 0.41 and p=0.39, respectively). GA and BW were also correlated with the presence of organomega-

ly (p = 0.009 and p = 0.45, respectively). The average total cholesterol (TC) level was 1485.52±1504.21 mg/dl (range: 70-7000), and the average triglyceride (TG) level was 16268±14578.09 mg/dl (range: 1000-64956). The TG level was found to be associated with the stage of LR (p=0.46). In addition to the case discussed, there were seven other premature neonates (GA<38) with LR, five of whom also had ROP, with two undergoing laser photocoagulations. Treatment strategies of LR varied, with dietary modifications and lipid-lowering medications showing some efficacy.

Conclusion: Lipemia retinalis is a rare condition that can occur in infants and neonates. Early recognition and management of underlying lipid disorders are crucial in preventing long-term complications. Further research is needed to investigate possible long-term impacts on visual development and optimal treatment strategies for LR in this population.

Keywords: Lipemia retinalis; neonate; infant; chylomicronemia; hypertriglyceridemia; lipoprotein lipase deficiency

Introduction

In 1880, Heyl provided a detailed description of a case of lipemia retinalis (LR) for the first time [1]. LR is an ocular manifestation of hypertriglyceridemia (HTG). Fundoscopic feature is creamy-white discoloration of the retinal vessels, involving peripheral vessels in mild cases which extend to central vessels in severe ones [2].

Typically, LR does not interfere with the visual acuity but is concerned due to the possible associated fatal but easily treatable metabolic disorders, [2] particularly since LR may precede these conditions [3].

Here in, we present a premature newborn diagnosed with LR during screening for retinopathy of prematurity (ROP). Furthermore, the current article delineates various clinical aspects of LR through a comprehensive review of literature indexed in PubMed or Google Scholar, with a specific focus on the unique considerations in infants and newborns.

Case Report

A 44- day-old boy, born to non-consanguineous parents with a gestational age of 34 weeks and a birth weight of 1980 grams following an uneventful delivery, was referred to us by a local health center for retinopathy of prematurity (ROP) screening. He has been exclusively breastfed and hospitalized in neonatal intensive care unit (NICU) for the management of respiratory distress syndrome (RDS) and jaundice.

Examination of anterior segment of both eyes was unremarkable. The fundus examination revealed fully vascularized retina, dilated tortuous creamy-white retinal vessels, yellowish optic discs and peripapillary atrophy. The distinction between arteries and veins was only possible due to the larger caliber of veins. There were no signs of lipid extravasation, exudative hemorrhage, vascular sheathing or optic disc swelling. The clinical diagnosis of LR was suggested. (Figure 1)

Immediate consultation with pediatric metabolism specialist was requested. Laboratory investigation revealed a grossly lipemic specimen (4+/4+). In addition, the blood sample taken in two-week-old for hypothyroidism screening had showed an elevated viscosity.

The serum triglyceride (TG) level was 1350 mg/dL (normal range: <150 mg/dL) and serum total cholesterol (TC) was 4600 mg/dL (normal range: <150 mg/dL). The blood tests were otherwise within normal limits for liver, kidney, hematologic, and endocrinologic functions. A thorough physical examination to investigate other manifestations of hyperlipoproteinemia did not reveal any symptoms such as hepatosplenomegaly or xanthomas.

The parents underwent laboratory examinations, revealing the following results: The mother had a TC level of 197 mg/dL and TG level of 508 mg/dL, while the father had a TC level of 370 mg/dL and TG level of 293 mg/dL. There was no history of lipid disorders in other family members.

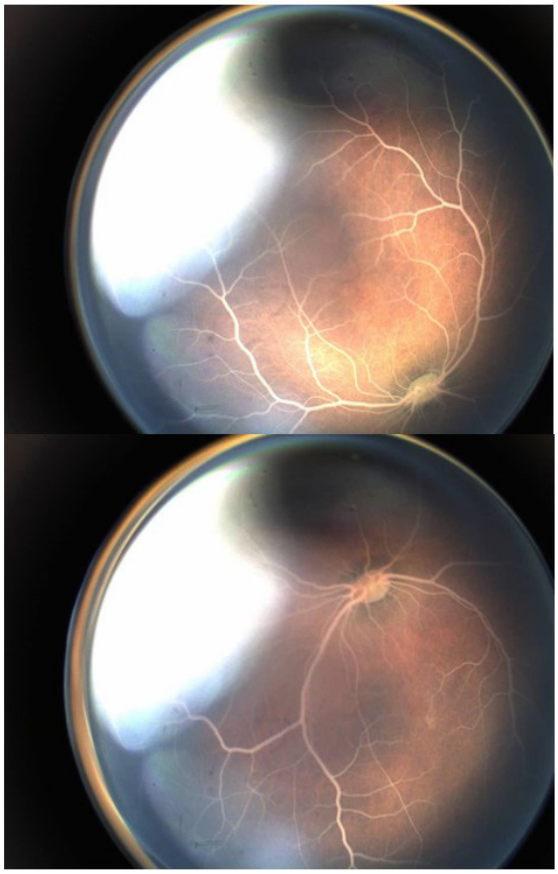

Figure 1: RetCam® (Clarity Medical Systems Inc., Pleasanton, CA, USA) imaging of the right eye (top image) and left eye (bottom image), demonstrating creamy white retinal vessels extending to the optic disc. The disc displays a yellowish hue, with the presence of peripapillary atrophy.

The baby was then switched on skimmed milk as a tight low-fat diet. Serum TG and TC gradually decreased to normal range within five weeks and funduscopic manifestations of LR regressed. The parents were advised to continue the low-fat diet and close follow-up visits by a metabolic disorder specialist.

A written informed consent was obtained from the patient's parents to illustrate the images and provide a report.

Discussion

A thorough explanation of the various clinical aspects of LR is presented through a comprehensive review of articles sourced from PubMed and Google Scholar.

Epidemiology

The precise epidemiology of LR is still uncertain, but some of the underlying causes have been identified. Familial HTG, caused by a deficiency in lipoprotein lipase (LPL), leading to elevated levels of chylomicrons in the blood, is highly uncommon, with a prevalence of less than 1 in 1 million in the United States and higher in other nations [2].

Familial combined hyperlipidemia, the other associated risk factor, is estimated to have a prevalence of 1% to 2% in the general population.[4] Approximately 1.7% of the total U.S. population were estimated to have severe HTG (500 to 2,000 mg/dl), with a majority being men (75.3%), non-Hispanic whites (70.1%), and aged 40 to 59 years (58.5%). Diabetes and hypertension were associated with 14% and 31.3% of cases of HTG, respectively [2, 5].

Clinical Manifestations

LR is a retinal pathology characterized by milky-creamy whitening of the retinal vessels due to chylomicronemia. Initially the symptoms are observed in the thinner vessels of peripheral retina; however, pathognomonicly, the posterior pole is involved when plasma TG levels exceed 28 mmol/L or 2,500 mg/dl.[6-9] As the picture fades from the fundus, the changes occur in reverse order [10].

The fundus background is variably lightened due to the choroidal circulation [11], and at levels surpassing 5000 mg/dL, the fundus takes on a salmon-colored appearance.[3, 6, 12] However, some authors defend that elevated levels alone are not enough to result in the appearance of a lipemic serum [13] or LR. They propose that alterations in hematocrit and transparency of retinal and choroid vessels should be taken into account.[12] For instance, Lai et al. suggest that the serum TG alone may not be the sole determinant of retinal manifestations, as normalization of retinal appearance may occur despite having a serum TG level still far more than 2500 mg/dl or the creamy-white discoloration may persist despite a decrease in serum TG level to below 2500 mg/dl [14]

Benson et al. reported dynamic retinal vessels color change during ocular compression from white to coral pink using a RetCam as a result of disruption of laminar flow and the intermixing of larger erythrocytes and smaller chylomicrons in a patient with LR [15].

The grading system for LR was stablished by Vinger et al.[8] In stage 1 (mild) there are creamy-white vessels isolated to the periphery, in stage 2 (moderate) creamy vessels extend towards the optic disc, and in stage 3 (marked) all retinal vessels become cream-colored and the posterior pole turns salmon-colored.[16]

Other associated ocular manifestations of elevated serum TG are lipemic aqueous, corneal arcus, corneal opacification, lipid keratopathy, xanthelasma and xanthomas (periorbital, conjunctival, iris, retinal or choroidal).[17] Moreover, retinal vein slugging and red cell aggregation,[3] uncommonly branch retinal vein occlusion with a marked exudative response in adults,[18] exacerbation of co-existing diabetic macular edema and diabetic exudative maculopathy [19] and multiple visible emboli in the first and second order of arteries has also been reported [20].

Etiology and Pathophysiology

Isolated HLP without accompanying HTG does not present with LR.[6-9, 18, 21-23] Chylomicrons, the largest lipoproteins (100-1000nm) transport dietary triglycerides from the intestine to the bloodstream. They are rapidly cleared from the blood, and their high TG content is related to elevated plasma TG levels and LR, as TG-laden chylomicrons scatter the light in retinal vessels besides smaller lipoproteins are transparent and do not scatter the light [6, 18].

Severe HTG can either be a primary familial condition like familial chylomicronemia syndrome (FCS) due to apolipoprotein C-II deficiency, LPL deficiency, and endogenous circulating low-density lipoprotein inhibitor, [6, 24] or can occur as a result of systemic disorders like diabetes mellitus, hypothyroidism, nephrotic syndrome, biliary obstruction, alcoholism [11], lipid storage diseases,[16, 25] high fat ketogenic diet [26] or decompensating hyperlipidemia during chemotherapy under accompanying treatment with dexamethasone [27] or asparaginase [28], using protease inhibitors in patients infected with human immunodeficiency virus (HIV),[29] acquired anti-apo C-II antibody[24] or following bone marrow transplant [7].

The most common underlying cause in both adults and children, but not infants and newborns, is diabetes mellitus. This has led some authors to categorize LR into diabetic and non-diabetic cases. The most common underlying cause in infants and newborns is FCS due to LPL deficiency. Typically, about 25% of cases of FCS are diagnosed during infancy [30, 31]. Differential diagnoses for FCS include Familial dysbetalipoproteinemia, characterized by elevated levels of cholesterol and triglycerides to a similar extent, typically presenting in adulthood with tuberoeruptive xanthoma. Familial HTG, on the other hand, presents without xanthoma, showing increased triglycerides but normal cholesterol levels. Additionally, Familial combined hyperlipidemia is characterized by higher cholesterol levels compared to triglycerides, without xanthomic eruptions [31].

As mentioned, the most commonly affected gene is lipoprotein lipase-1 gene (LPL), which is responsible for hydrolyzing circulating TG for tissue uptake [32]. LPL deficiency, a rare autosomal recessive disorder with an incidence of 1 in 1,000,000, is uncommon in HLP. LPL which is found in vascular endothelium, is the key enzyme in breaking down the chylomicrons into glycerol and free fatty acids and its deficiency leads to chylomicron accumulation.[12] Various gene mutations of LPL have been documented, including Asp9Asn, Gly188Glu, Pro207Leu, Asp250Asn, Asn291Ser, Ser447X, Pro214Ser, and others [33].

Mutations in other genes that control maturation, transport or polymerization LPL such as APOC2, APOAV, LMF-1, GPI-HBP-1, could also play a role. [32] Definite attributing mutations such as homozygous p.G215E mutation in the LPL gene have been previously reported to be involved in a 6-week-old full-term newborn with HTG and LR [34].

Nevertheless, in approximately 30% of patients with FCS, the causal variant remains unidentified [32]. In addition, genotype--phenotype correlations have not been determined, as there is no significant association between the type or location of the mutation, age at diagnosis, lipid levels, and the severity of symptoms [35]. Although some studies [36] have indicated that the genetic basis of childhood HTG is not limited to a specific type of HLP, other studies [35] have suggested that TG levels were elevated in compound heterozygotes compared to homozygotes. Hence, it seems that there may be additional factors beyond LPL polymorphism determining TG levels [34].

Ophthalmic Impacts

Though various electroretinographic alterations including decreased a- and b-waves in both cone and rod responses, [22] borderline-delayed implicit times to a 30-Hz flicker,[37] have been reported in LR, it only impacts visual acuity in exceptional cases.[27, 38-40] Even in these instances, full restoration of vision is achieved through medical intervention [27, 38] and it is suspected to play role in increasing the risk of retinal vascular accidents[18].

Waleed K Alsarhani et al. in a cross-sectional case series have reported that there was a notable change in retinal oximetry and retinal blood flow in both the resolved and untreated groups with LR. The increase in retinal blood flow and oxygen saturation could explain why visual acuity and function are maintained despite the fundus changes seen in LR. [41] However, it is still uncertain whether future retinal function and vision development could be affected in infants with severe HTG.

Ophthalmic Investigations

LR is diagnosed based on clinical manifestations. An investigation into an underlying cause through laboratory tests and assessment of potential associated complications, such as pancreatitis and coronary artery disease, is warranted. Further ophthalmologic evaluations are deemed unnecessary due to inconclusive results from prior studies.

Various electroretinographic alterations including decreased a- and b-waves in both cone and rod responses, [22] borderline-delayed implicit times to a 30-Hz flicker,[37] are reported previously.

Previous multimodal studies reported hyper reflections from both arteries and veins in fundus autofluorescence (FAF) [39, 42,

43] and optical coherence tomography (OCT) has revealed multiple high point-like reflections in the retinal sections, corresponding to various calibers of blood vessel sections [39, 42] and medium reflections were observed in the large vessels of the choroid and a prominent middle layer membrane sign [43]. While some authors reported Fundus fluorescein angiography (FFA) and OCT angiography (OCTA) showed no notable alterations [39], some others demonstrated slowed choroidal and retinal flow [43].

Associated Complications

Timely identification of LR is essential, as persistent DLP may lead to associated potentially lethal morbidities including early atherosclerosis and coronary artery disease, acute or recurrent pancreatitis and consequent pancreatic insufficiency, and hepatic failure, especially in preterm and term babies. Pancreatitis is the most worrisome complication in both pediatric and adult populations.[3, 9, 21, 23, 34, 44] LR is an important clinical indicator of HTG because initial asymptomatic increase in TG levels can delay the treatment of these life-threatening disorders [3]. Childhood HTG may lead to failure to thrive (FTT) or not.[45, 46].

Management and Treatment

While treatment is essential for addressing the systemic hazards of HTG, typically no treatment is needed for LR itself. Once TG levels normalize, the clinical ocular findings of LR should promptly improve [3, 6].

Chylomicronemia can be managed at first by strict adherence to fat restriction, consisting of 10% to 15% of daily caloric intake from fat, and by reduction of consumption of saturated and trans fats. Medium-chain fatty acids can be included in the diet as they are absorbed directly into portal circulation and do not require chylomicron formation [6].

Pharmacological interventions are required to maintain TG levels <2,000 mg/dL in order to reduce the risk of pancreatitis, especially if dietary interventions are unsuccessful in managing HTG. It is important to note that lipid-lowering drugs like statins, fibrates, and niacin are typically not effective in individuals with LPL deficiency [47]. Current pharmacological interventions may involve fibrates and omega-3 fatty acids, but the focus is on biotechnological agents that address the molecular disturbances of the condition (e.g., an antisense oligonucleotide against apoC-III (volanesorsen), a monoclonal antibody against angiopoietin-like protein-3 (evinacumab)) [32].

It is suggested that during the period when normal levels of plasma fat are being restored, administering a low dose of heparin infusion can aid in preventing obstruction in small blood vessels [21].

Some authors have reported the utility of plasma exchange, or when unavailable, exchange transfusion in infantile LPL deficiency in rapid alleviation of pancreatitis, lipemic indicators, alongside rapid (within 3 days) disappearance of LR [48-50]. And LDL apheresis (a method to eliminate unwanted LDL from blood stream using a machine that pumps patient's blood through a filter which selectively removes LDL) is reported to effectively improves lipemic indicators and normalize the retinal appearance in an adult patient [51]. The majority of reports on apheresis for HTG focus on plasmapheresis, which typically results in a 60-70% reduction in TG concentrations after a single session [52].

Lastly, studies on gene therapy for patients with LPL deficiency have been conducted as a potential treatment option [53].

Lipemia Retinalis in Infants and Neonates: A Case-Based Review of Literature

All articles indexed in Google Scholar and PubMed containing the terms "infant", "newborn", "pediatrics", hypertriglyceridemia," "hyperchylomicronemia," and "lipemia retinalis" were selected for inclusion in the study. Articles with non-English full text were excluded. A total of 44 articles were included, and our case information was added as the 45th case. Case information was

extracted, and patient age expressed in days or months was converted to weeks. In instances where the "full term" or “term” was mentioned, the gestational age (GA) was considered to be 40 weeks. Triglyceride and total cholesterol units expressed as mmol/l were converted to mg/dl. All data was entered into SPSS 24 to provide an analysis through a case-based review of literature.

Table 1 illustrates the clinical characteristics of newborns and infants with LR as previously reported in the literature.

Table 1: Clinical characteristic of previously reported patients with Lipemia Retinalis

article	*Year*	*Sex/ Age*	*consanguinity*	*FH*	*GA*	*GW*	*LR stage*	*Associated complications*	*TC/TG*	*Underlying cause*	*management*
T. Öztürk [9]	2021	13 w/ female	Neg	Neg	26	680	3	stage 1 zone 2 ROP, developed bilateral stage 3 zone 2 ROP with plus disease	TG>10000		laser photocoagulation at 35w for ROP/ strict low-fat diet
Alon Zahavi [6]	2012	12 w/ male	4th degree	Neg	40	NA	3	Hepatomegalyxanthoma	TC:1700TG:24500	LPL deficiency	Breast feeding stopped
Neha C. Jain [79]	2017	1 m/ female	4th degree	NA	NA	NA	3	history of umbilical discharge	TC: 7000TG: 8530	LPL deficiency	Skimmed milk
Cody Lo [80]	2023	40 d/ female	NA	NA	NA	NA	3	Melena, rectal bleeding	TG:38709	LPL deficiency	NA
Shinkre [7]	2019	27 d/ male	3ed degree	Pos	40	NA	3	bleeding from the umbilicus and left ear since 1 day after birth/ hepatospleenomegaly	TC:4560TG:10350	FCHL	skimmed milk / lipid lowering agents
Vidanapathirana DM [81]	2017	12 m/ male	Neg	Pos	38	NA	NA	hepatosplenomegaly	TC:370TG:4910	LPL deficiency (compound heterozygous)	low-fat diet/ fenofibrate/ omega-3 fish oil
Cypel M [12]	2008	35 d/ female	3ed degree	pos	40	3070	NA	enterorrhagia (ulcerated lesions in the colon) / hepatosplenomegaly/ xanthomas	TC:1000TG: 3000		Breastfeeding stopped/Skimmed milk
Ikesugi [72]	1996	4 w/ male	NA	Neg	31	816	2	Bilateral stage 1 zone 2 ROP	TC:594TG:14722	Low LPL at 6w which normalized at 8m of age	MCT milk, cow’s milk
Jain A[23]	2017	2 w/ female	Neg	Neg	30	1070	3	stage 3 ROP in zone II with plus at 36 w	TC:136TG:4736		laser photocoagulation of both eyes/ MCT milk along with breastmilk
Yin H Y [34]	2016	6 w/ female	NA	Neg	40	NA	3	emesis and blood-streaked stools/vulvar xanthomas	TG:27988	LPL deficiency	breast milk and adequate intravenous hydration combined with Enfaport and then ceasing breast milk and starting Monogen
Groom J J [16]	1950	7 m/ male	NA	NA	NA	NA	2	Hepatosplenomegaly	TC:448TG: 5242	Niemann-Pick disease	low-fat diet
Capitena CE [48]	2016	7 w/ female	NA	NA	NA	NA	3	fever, emesis and feeding intolerance, pancreatitis/ hepatomegaly	TC:1807TG:15078	LPL deficiency	double exchange transfusion
Uwaydat SH [82]	2000	2 m/ female	3ed degree	PosLR stage 1 in her sister	40	NA	3	Anemia, Poor breast milk intakeEruptive xanthoma, hepatosplenomegally, pancreatitis, nephrosisPinkish discoloration of conjunctiva and iris vessels	TC:770TG:30000	HLP type 1	Skimmed milk/ MCT
Benson M [15]	2018	6 w/ hispanic female	Neg	NA	NA	NA	2	high levels of potassium, respiratory acidosis and high lactate	TC:770TG>8000	HLP type 1	MCT formula/sunflower oil supplementation
Behera JR [31]	2020	40 d/ female	Neg	pos	40	2800	NA	poor feeding/ hepatosplenomegaly/ eruptive xanthomas over knee, face and buttocks	TC:1467TG:5997	LPL deficiency	Fenofibrate, MCT, skimmed milk
Rotchford AP [71]	1997	14 w/ female	NA	NA	26	960	3	stage 3 ROP in zone III was observed in the left eye at 37 w	TG:6908	HLP type 1 (no LPL deficiency)	Low fat diet, MCT

Verma R[78]	2022	45w/ female	Neg	NA	30	540	3	Sepsis, poor weight gain and poor feedingstage 3 ROP in zone II in both the eyes with no plus disease	TC:1200TG:2793		low fat skimmed milk/ lipid lowering agents patient died
Hayasaka S [73]	1985	female	3ed degree	Neg	40	3280	3	Eruptive xanthomas in upper eyelids	TC:400TG:15000	LPL deficiency	Low fat diet
Cermàkovà I [21]	2010	female	Neg	pos	40	3430	NA	fever and feeding problem, biliary vomitingmultiple facial xanthomas	TC:820TG:12380	LPL deficiency	skimmed milk/ low dose heparin
Shah MH [47]	2018	23 d/ female	3ed degree	Neg	39	3550	NA	fever, vomiting, pancreatitis	TG:10300	LPL deficiency	Skimmed milk/ MCT/Gemfibrozil
Kose E [83]	2018	46 d female	3ed degree	Neg	40	NA	NA	feeding problems/ hepatomegaly	TG:6295	apo C-II deficiency	Breastmilk stopped/low-fat diet/MCT/omega-3 fatty acid supplement
Ghoor S [84]	2018	7 w/ female	NA	NA	34	1900	NA	Feeding problems, dark red blood in the stool/acute respiratory distress syndrome/xanthomata, on the face and the wrists	TC:726TG:64956		double exchange transfusionbreastmilk stopped/MCT/Low fat diet
Schoeneberg LA [85]	2017	6 d/ male	NA	NA	NA	NA	NA	fever and a rash	TC:1000TG:23900	LPL deficiency?	Low fat diet/ MCT
Soto AG[86]	2015	11 w/ male	Neg	Neg	40	3740	NA	coffee-ground emesis, melena and a papular rash	TC:738TG:43980	LPL deficiency(compound heterozygote)	Breast milk stopped/ MCT
Kolářová H [87]	2014	2.5 m/ female	NA	Pos	40	2700	NA	loss of appetite, constant crying and abdominal distention with ascites/ splenomegalyenlarged kidneysLiver biopsy: steatosis with mild fibrosis	TG:1089	LPL deficiency	Low fat diet/ MCTpolyunsaturated fatty acids (PUFAs), vitamins A, E, D and calcium
Kolářová H [87]	2014	2 m/ male	NA	Neg	40	4370	NA	recurrent ear and skin infections, perianal mycosis and abdominal distension/ hepatosplenomegaly	TC:684TG:13639	LPL deficiency	low-fat diet Since the age of one year
Sriram CS [4]	2005	4 m/ male	Neg	Pos	NA	NA	NA	Fever, pneumonia	TC:677TG:10400	FCHL	Low fat diet
Sowjanya SV [88]	2017	5 d/ male	3ed degree	Neg	38	3000	NA	Icterus in day 4/ Hepatosplenomegalyelevated apolipoprotein A1	TC:2340TG>10000	HLP type1	Skimmed milk/ MCT
Ashraf AP [70]	2017	36 d/ female	Neg	NA	40	2550	NA	pseudoacidosis, pseudohyponatremia, and severe anemia, elevated WBCliver steatosis	TC:1295TG:24318	LPL deficiency	packed RBC due to anemiainsulin along with dextrose for 48 hoursTolerex mixed with Liquigen
Wani K [59]	2015	10 d/ female	3ed degree	pos	40	NA	NA	Poor feeding/ hepatosplenomegaly	TC:1236TG:2132		Skimmed product/ MCT/ Olive oil
Chaudhury D [89]	2015	3 m/ female	Neg	Pos	NA	2880	3	respiratory distress	TC:914TG:4949		skimmed milk/ Questran sachets (cholåstyramine resin and sucrose)Atorvastatin
Buonuomo PS [90]	2015	3 d/ female	Neg	Neg	40	3100	NA	Mild jaundice	TC:130TG:1667	LPL deficiency (compound heterozygous)	infusion of isotonic intravenous solution/ low-lipid formula diet
Nampoothiri S [30]	2011	38 d/ male	Neg	NA	NA	3500	NA	Fever / Hepatomegaly and abnormal liver function tests	TC:659TG:8874		Low fat diet/ skimmed milk/ MCT
Avis HJ [91]	2010	3 m/ female	Neg	Neg	40	NA	NA	vomiting, loose stools and apparent abdominal pain, alternating yellowish and pale skin color/ mild hepatomegaly	TG:22250	LPL deficiency	A nearly fat-free diet (Basic-F, nutricia), supplemented with essential fatty acids
Shankar KN [92]	1997	3 m/ female	NA	NA	NA	NA	NA	Bronchopnemonia		LPL deficiency	
De S[93]	2015	2.5 m/ male	3ed degree	pos	NA	NA	NA	black tarry stool with pallor and distension of abdomen/ multiple xanthomatous eruption (over knees and extensor aspect of the limbs)/ hepatosplenomegaly, abnormal LFT	TC:3820TG:28980		vitamin K1 and blood transfusioncontinued breastmilk/ MCT

Mahapatra SK [94]	2020	25 d/ female	Neg	Pos	40	3500	3	greenish black stools/ pancreatitis/ hepatosplenomegaly	TC:1912TG:44000	FCHL	antibiotics, IV fluids, dietary modifications/ breast feeding stopped
Chaudhary NK [61]	2018	28 d/ female	Neg	Neg	NA	2700	NA	fever and cough/ hepatomegaly	TC:1708TG:13812	LPL deficiency	fat restricted milk, MCT and fat-soluble vitamins
Heath O [95]	2024	10 w/ female	consanguineous	NA	40	NA	NA	fever, vomiting, and failure to thrive/ hepatomegaly/ Eruptive xanthomas on torso/ pancreatitis/ generalized pallor/ hypoalbuminemia		LPL deficiency	Enteral feeding suspended for the first 24 h/ IV fluids/insulin heparin, breastfeeding stopped, Monogen*(then paused (day 2–3) and replaced with fat-free parenteral nutrition)
Srinivas RK [46]	2021	28 d/ male	NA	Pos	37	NA	NA	RDS/ hepatosplenomegaly/ pancreatitisraised hemoglobin with reduced hematocrit	TC:70TG:40000	Familial HTG	Gemfibrozil, fat soluble vitamins, MCT, docosahexaenoic acid
Pawal P [57]	2023	1 m infant	consanguineous	Neg	40	NA	NA	recurrent vomiting, diarrhea, hematocheziaanemia/ hepatosplenomegaly/ pancreatitis	TG:36400	Familial HTG	dietary modifcations, fenofibrate Docosahexaenoic acid (DHA) Eicosapentaenoic acid (EPA)
Mess AM .[96]	2020	3 m infant	NA	Pos	NA	NA	NA	History of GI bleeding/ high fever, cough, breathlessness/ hepatosplenomegaly/ pancreatitis	TC:361TG:2146	HLP type 1	Simvastatin/ low fat diet/ exclusive breastfeeding
Jadhav SS [97]	2022	6 m/ male	3ed degree	Neg	NA	2200	NA	History of recurrent episodes of acute abdominal colic followed by green-colored vomiting and loose motions/ acute pancreatitis, splenomegaly, mild asciteslipemic lumbar puncture	TC:1040TG:6400		Low fat dietAyurveda
Ozdemir M [98]	2003	NA	NA	NA	NA	NA	NA		TC:1470TG:29000	Familial HTG	

Abbreviations: w: weeks/ m: months/ d: days/ NA: not applicable/ Neg: negative/ Pos: positive/ TC: total cholesterol/ TG: triglyceride/ LPL: lipoprotein lipase/ HLP: hyperlipoproteinemia/ HTG: hypertriglyceridemia/ FCHL: familial combined hyperlipoproteinemia/ LR: lipemia retinalis/ ROP: retinopathy of prematurity/ MCT: medium chai triglyceride/ RDS: respiratory distress syndrome/ GI: gastrointestinal/ IV : intravenous

The scarcity of case reports may be attributed to the absence of regular fundus examinations and the infrequency of clinical symptoms presenting at a young age. Absence of noticeable symptoms and involvement of peripheral retinal vessel contribute to the underdiagnosis of this condition. Conducting a thorough examination of the peripheral retina during the diagnosis of HLP may uncover a higher incidence of this condition.

Demographics

Among the 45 cases included in the study, 27 (60%) were female, 15 (33.3) were male, and the gender of three cases (6.7%) was unspecified. The mean age of infants at the time of evaluation and diagnosis of LR was 10.11±10.68 weeks. (range: 3 days- 12 months)

Gestational age (GA) and birth weight (BW) were determined in 30 and 23 cases, respectively. The average GA and BW were 37.43±4.41 weeks (range 26-40) and 2535.48± 1086.27 grams (range 540- 4370), respectively. Unfortunately, a baby girl born at 30 weeks weighing 540 grams passed away four months after birth.

Underlying Cause

Primary HTG is caused by various genetic defects affecting triglyceride metabolism. These genetic defects can be classified as either common or rare variants within the Frederickson classification system. These include chylomicronemia (type I), familial hypertriglyceridemia (type IV), and the more severe combined hypertriglyceridemia and chylomicronemia (type V). Hepatic lipase deficiency can also lead to a similar combined hyperlipidemia.

According to our study, Type 1 hyperlipoproteinemia (76.4%) was identified as the most prevalent underlying cause, with 21 cases (46.7%) attributed to lipoprotein lipase (LPL) deficiency, 1 case (2.9%) to apolipoprotein C2 deficiency, and four cases categorized as unspecified (3 cases not evaluated and 1 case normal). Four (11.7%) patients were diagnosed with familial combined hyperlipoproteinemia (FCHLP), while two (5.8%) were diagnosed with familial hypertriglyceridemia (FHTG). One patient was diagnosed with Niemann-Pick disease, and another was a premature infant who had low LPL levels at 6 weeks of age, which normalized by 8 months of age. A definitive diagnosis was not established in 11 cases, accounting for 32.3% of the total cases.

Familial Chylomicronemia (Type I HLP) is a rare autosomal recessive disorder caused by mutations affecting apoB lipoprotein clearance, typically presenting with acute pancreatitis in childhood. Familial HTG (Type IV HLP) is an autosomal dominant disorder characterized by elevated plasma TGs, often accompanied by slight increases in cholesterol and low HDL levels. HTG Type V is more severe, with elevated levels of chylomicrons and VLDL particles, often exceeding 1,000 mg/dL [46].

In infants, the primary cause of T1HLP is typically attributed to mutations that result in the loss of function in LPL or related proteins like apolipoprotein C2, apolipoprotein A5, lipase maturation factor-1, and glycosylphosphatidylinositol-anchored high-density lipoprotein binding protein 1 [54-56]. The most likely identified risk factor for the germline mutation in the LPL gene is the consanguineous relationship of the parents, [57] as FCS is inherited in an autosomal recessive manner, and a positive family history necessitates screening of other family members (parents and siblings). Even if the lipid profile appears normal, regular monitoring with lipid profile assessments is recommended [58, 59].

According to our review, the consanguinity status was unspecified for 17 patients. Out of the remaining cases, 45.1% (14/31) were identified as relatives, with 10 out of 14 (71%) being third-degree consanguineous and 2 out of 14 (14.2%) being fourth-degree consanguineous. The degree of consanguinity was not specified for 2 patients.

Because of the genetic origins of these conditions, there is a potential for familial predisposition to occur. Our results demonstrated family history of susceptibility, either through history taking or laboratory evaluation, was mentioned in 31 cases. Among these, 16 cases (51.6%) had a first-degree relative with an abnormal lipid profile. In only one case, HLP type 1 and LR stage 1 were observed in the patient's elder sister.

Presentation

Almost all the cases are diagnosed accidentally when evaluating for ROP, non-accidental trauma, sepsis, etc. Lipemic serum addressed the physicians to evaluate serum lipid profile. The most common symptom prompting evaluation was vomiting or poor feeding in 13 (36.1%) of cases, followed by fever or other manifestations of sepsis or infection in 11 (30.5%) of cases. 7 (19.4%) patients exhibited bleeding episodes including bleeding ear or gastrointestinal bleeding. 5 (13.8%) patients were incidentally diagnosed during funduscopy for ROP screening, or through lipemic serum identified during routine laboratory tests in the early postnatal period. All patients exhibited lipemic serum, with one also experiencing a lipemic lumbar puncture.

In 18 cases (40%), the stage of LR was specifically identified, with 4 cases classified as stage 2 and 14 cases classified as stage 3. In the remaining cases, either the patient had LR without a specified classification, or the fundus description was insufficient

for determining the stage. There were no reports of stage 1. The absence of reports of stage 1 may be attributed to misdiagnosis with other conditions, incomplete or imprecise peripheral funduscopy, or it might not have been deemed as significant or interesting for clinicians to document. Performing a detailed assessment of the peripheral retina when diagnosing HLP may reveal a higher prevalence of this condition.

FCS, as the most common underlying cause of infantile LR, is characterized by severe HTG, leading to symptoms such as abdominal pain, recurrent acute pancreatitis, eruptive cutaneous and visceral xanthomata, hepatosplenomegaly. Anemia has been documented in previous cases, as well as in instances where gastrointestinal bleeding resulted from visceral xanthomas in an infant. However, it is important to note that anemia in these cases may also be partially misleading or falsely represented [54, 60]. It can lead to neurological manifestations and dyspnea [61]. Overall, the presentation of FCS during infancy can vary and may include additional signs such as pallor, jaundice, irritability, and diarrhea. These symptoms can manifest at different times and with varying degrees of severity [58, 59].

In a retrospective study on 15 children with severe HTG, Kuthiroly et al. reported that hepatomegaly (15/15), splenomegaly (9/15) and LR (14/15) were common findings and LR proved to be a valuable non-invasive diagnostic tool.[62] Now according to our results, in the context of LR, xanthoma was present in 10 patients (22.2%), organomegaly in 23 patients (51.1%), and pancreatitis in 9 patients (20%). None of the ocular manifestations of HTG were present in all cases, except for one case that exhibited pinkish discoloration of the conjunctiva and iris vessels.

The GA demonstrated a statistically significant correlation with the presence of xanthoma and pancreatitis. ($p = 0.41$ and $p=0.39$, respectively). Newborns devoid of xanthoma and pancreatitis exhibited a mean GA of 36.63± 4.93 and 36.95± 4.80 weeks, respectively, whereas those presenting with xanthoma and pancreatitis manifested a mean GA of 39.33± 2 and 39.33± 1.21 weeks, respectively.

The GA and BW were found to be correlated with the presence of organomegaly in the study population ($p = 0.009$ and $p = 0.45$, respectively). Neonates without organomegaly had a mean GA of 35± 5.51 weeks and a mean BW of 2176.85± 1183.05 grams, while those with organomegaly demonstrated a mean GA of 39.56± 0.96 weeks and a mean BW of 3093.33± 628.82 grams.

These associations may be elucidated by the hypothesis that term infants and those with higher birth weight experienced prolonged exposure and higher fat intake, resulting in a more severe degree of hypertriglyceridemia.

The data for TG and TC levels was available for 36 and all 45 patients, respectively. The average TC level was 1485.52± 1504.21 mg/dl (range: 70-7000), while the average TG level was 16268± 14578.09 mg/dl. (range: 1000-64956)

The TG level was found to be associated with the stage of LR. ($p=0.46$) Individuals in stage 2 exhibited a mean TG level of 7328.50± 5633.55, whereas those in stage 3 demonstrated a mean TG level of 17395.78± 13347.57.

No significant associations were identified between TG or TC levels, LR stage, and age at presentation, GA, GW, consanguinity, or a family history of dyslipidemia.

Management

Managing infants with HTG in the acute phase poses challenges. Fasting is a key component of the management strategy as it halts the production of additional chylomicrons, enabling the gradual clearance of existing chylomicrons from the circulation [63, 64].

Not all authors have described the treatment administered during the acute phase of HTG. However, in two patients, a combination of low-dose heparin, insulin, and dextrose was used to manage extremely high TG levels. The administration of intravenous insulin and glucose can help reduce serum TG levels by stimulating any remaining LPL activity. However, it is important to note that the effectiveness of this approach may be constrained in cases of absolute LPL deficiency [65, 66]. Insulin presents a unique and cost-effective treatment option for individuals with severe HTG, aiding in the prevention of both acute and chronic complications.

Exchange transfusion (ET) instead of plasmapheresis, was utilized as an additional treatment in cases of acute and extremely high TG levels to prevent the occurrence of pancreatitis. Plasmapheresis may not be feasible in many centers during the neonatal period due to challenges like hemodynamic instability and technical limitations. Though the effectiveness and safety of exchange transfusion therapy as a viable option for the acute management of HTG in neonates is recommended [67].

At present, there is no consensus for a standard treatment of infants presenting with severe HTG. The primary treatment approach involves maintaining a diet where fat intake is limited to 10% to 15% of total energy.[68] Breast milk, which typically supplies 50% of energy from fat,[69] must undergo fat removal through centrifugation before being administered or must be discontinued. Medium-chain triglycerides (MCTs) in the diet are advantageous as they are absorbed directly into the portal circulation for hydrolysis without forming chylomicrons.[70] High MCT formula with [71] or without [72, 73] breastfeeding has been used to manage infants with TG level <170 mmol/L. Yin et al. suggest discontinuing of breastfeeding in extremely high TG level (>300 mmol/L), [34] since the elevated levels of long-chain fatty acids in breast milk could potentially lead to increased serum TG levels in individuals with severe HTG [34, 74]. Our review exhibited that three patients continued breastfeeding.

Some of suitable formulas for patients with T1HLP include Tolerex (2% of total energy as MCT and LCT; Nestle), Vivonex Pediatric (25% of total energy as fat: 17.5% MCT, 7.5% LCT; Nestle), Monogen (24% of total energy as fat: 19.2% MCT, 4.8% LCT; Nutricia) and Vivonex RTF (10% of total energy as fat: 4% MCT, 6% LCT; Nestle). The primary objective of treatment is to prevent acute pancreatitis by maintaining serum TG levels < 1000 mg/dL [70].

In contrast to many documented cases showing benefits from MCT, Jain et al. reported a case of prematurity with LR, where the use of MCT resulted in a paradoxical worsening of HTG [23].

A homemade special formula utilizing locally accessible cereals and millets rich in crude fiber and low glycemic index, combined with MCTs, has been employed to effectively manage TG levels within acceptable ranges in older infants[75].

Lipid-lowering agents, such as fibrates or statins, were prescribed for a total of 8 (17.7%) patients. The use of niacin in infants with HTG is not advised due to potential toxicities, such as liver disease. HMG-CoA reductase inhibitors have varying levels of success in reducing TG levels. Data on the safety and efficacy of fibric acid derivatives in children is also scarce. The marine omega-3 fatty acids containing omega-3-acid ethyl esters have been shown to reduce VLDL production and serum TG levels by up to 50% or more [46].

An author claimed that Ayurveda, an alternative treatment, was effective in reducing TG levels.

Advances in understanding the molecular basis of chylomicronemia have led to the development of targeted therapies. LPL gene therapy is a specific treatment for the genetic disorder, while inhibitors of MTTP and DGAT1, antisense oligonucleotides targeting APOB, APOC3, and ANGPTL3 mRNAs, and other emerging pharmacological agents show promise for treating both monogenic and polygenic chylomicronemia. Monitoring ongoing clinical trials for these therapies is crucial to assess their effectiveness in managing FCS [76].

Lipemia Retinalis of Prematurity

In addition to our case, there are seven other premature neonates (GA<38) with LR, totaling eight instances in the study. Five were females, and three were males. Four individuals had a negative consanguinity status, while it was not applicable in the remaining four individuals. Two had stage 2 LR, four had stage 3, and the stage was unspecified for the remaining two. Only one case had Xanthoma and one another had both organomegaly and pancreatitis.

The underlying cause was specified for four cases. Two cases had type 1 HLP, one had familial HTG, and one had transient low Lipoprotein Lipase (LPL) levels that improved by the age of 8 months. In addition to routine treatment with skimmed milk and MCT, one patient underwent an ET, and another patient took a lipid-lowering agent.

Among the premature individuals, two had stage 3 ROP in zone 3, one had stage 1 ROP in zone 2, and two had stage 3 ROP in zone 3. Additionally, two individuals had plus disease. Two out of five individuals underwent laser photocoagulation for concurrent ROP, while three others were being followed up for it. The chance of coincidentally diagnosing LR during screening for retinopathy of prematurity (ROP) is extremely rare, as Ranjan has documented only one case out of 9,105 infants assessed [77]. This underscores the importance of early screening for ROP, which can facilitate prompt diagnosis and management of metabolic disorders. While acute HTG has not been associated with retinal neuronal and vascular toxicity, prolonged cases may lead to alterations in vascular morphology. These changes can complicate the diagnosis of plus disease and the management of ROP [78].

Ikesugi et al. first described LR of prematurity in 31 weeks neonate examined for ROP. Although the LPL activity was low at age of 6 weeks, it normalized at age of 8 months. The transient reduction of LPL activity was due to prematurity. Even though both ROP and LR were diagnosed simultaneously in this patient, the ROP exhibited gradual improvement before the HLP was addressed. This indicates that the LR was likely not a factor in the development of ROP [72].

Preterm infants and babies with intrauterine growth restriction (IUGR) may have a higher likelihood of developing LR because of significant risk factors for HTG, including reduced LPL activity, parenteral nutrition, and the use of MCT formulas, which are frequently given to low-birth-weight babies [9, 21, 23, 34]. The diagnostic aspect of LR in premature infants can be unique in that, due to the small size of the premature neonate, a sufficient amount of blood could not be drawn to determine TG concentration before LR was observed during fundus examination.

Conclusion

Dilated routine examinations can reveal different ocular and retinal pathologies including several metabolic disorders, even in very early stages prior to other systemic symptoms and signs.

As the early diagnosis of LR and multidisciplinary healthcare team is life-saving, it is crucial to conduct a systemic evaluation and relevant laboratory tests in patients with LR to identify the underlying cause, as high serum lipid levels can have fatal impacts. Additionally, evaluation of parents and siblings, genetic counseling, and providing dietary recommendations are essential in management of LR. Early genetic assessments during initial consultations will help inform the course of treatment and the outlook for the disease.

While existing literature indicates that fundus manifestations of LR may regress with proper treatment, the potential impact on future retinal function and vision development in infants with severe HTG remains uncertain. Further studies are warranted to assess the long-term impact of severe HTG and its treatment, not only on restoring normal retinal appearance but also on vision development.

Additionally, further research over an extended period is necessary to confirm the safety and efficacy of medications for treatment of HTG in pediatric patients.

Our study was constrained by the specific limitations inherent in a case-based review study. Laboratory tests were conducted using various methods and reported in diverse units. The presentation of data varied significantly among different authors, leading to notable discrepancies and missing data. Ongoing research using standardized study protocols is needed to assess primary HTG in infants.

Conflicts of Interest

The authors have no conflicts of interest to declare

Funding Sources

This study is not funded

Author Contributions

NK and HN contributed to data gathering, and drafting and approval of the manuscript

Data Availability

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

References

1. Heyl AG (1880) Intra-Ocular Lipæmia. Trans Am Ophthalmol Soc, 3: 54-66.

2. Mishra C, K Tripathy (2024) Lipemia Retinalis, in StatPearls. 2024, StatPearls Publishing

3. opyright © 2024, StatPearls Publishing LLC.: Treasure Island (FL).

4. Horton M, K Thompson (2011) Lipemia retinalis preceding acute pancreatitis. Optometry-Journal of the American Optometric Association, 82: 475-80.

5. Sriram CS et al. (2005) Familial combined hyperlipidemia in a North Indian kindred. Indian J Pediatr, 72: 987-9.

6. Christian JB et al. (2011) Prevalence of severe (500 to 2,000 mg/dl) hypertriglyceridemia in United States adults. Am J Cardiol, 107: 891-7.

7. Zahavi A, M Snir, YR Kella (2013) Lipemia retinalis: case report and review of the literature. J aapos, 17: 110-1.

8. Shinkre ND, UPS Usgaonkar (2019) Lipemia retinalis in a 27 day old neonate: A case report. Indian J Ophthalmol, 67: 954-7.

9. Vinger PF, BA Sachs (1970) Ocular manifestations of hyperlipoproteinemia. Am J Ophthalmol, 70: 563-73.

10. Öztürk T et al. (2021) Lipemia Retinalis Diagnosed Incidentally After Laser Photocoagulation Treatment for Retinopathy of Prematurity. Turk J Ophthalmol, 51: 313-6.

11. Davies WS (1995) Idiopathic lipemia retinalis. AMA Arch Ophthalmol, 53: 105-8.

12. Brown MS (1991) The hyperlipoproteinemias and other disorders of lipid metabolism. Harrison's Principles of Intemal Medicine, 1814.

13. Cypel M et al. (2008) Lipemia retinalis in a 35-day-old infant with hyperlipoproteinemia: case report. Arquivos brasileiros de oftalmologia, 71: 254-6.

14. Klintworth GK, A Garner (2008) Disorders of Lipid and Lipoprotein Metabolism, in Garner and Klintworth's Pathobiology of Ocular Disease, CRC Press, 1140-57.

15. Lai CC, CH Chang (2011) Lipemia retinalis with different therapeutic responses: A report of two cases. Taiwan J Ophthalmol, 11: 405-7.

16. Benson M et al. (2018) Dynamic Retina Vessel Color Change During Ocular Compression In Severe Lipemia Retinalis. Retin Cases Brief Rep, 12: S98-s101.

17. Groom JJ, CW Rucker (19950) Nondiabetic lipemia retinalis. Am J Ophthalmol, 33: 1238-40.

18. Gopal L et al. (2004) Hyperlipidemia in a poorly controlled diabetic presenting with lipemic aqueous and lipemia retinalis. Retina, 24: 312-5.

19. Nagra PK, AC Ho, JD Dugan (2003) Lipemia retinalis associated with branch retinal vein occlusion. Am J Ophthalmol, 135: 539-42.

20. Hinkle JW, N Relhan, HW Flynn (2018) Lipemia Retinalis, Macular Edema, and Vision Loss in a Diabetic Patient with a History of Type IV Hypertriglyceridemia and Pancreatitis. Case Rep Ophthalmol, 9: 425-30.

21. Wang P, EK Chin, DRP Almeida (2020) Lipemia Retinalis in a Patient with Familial Hypertriglyceridemia. J Clin Imaging Sci, 64.

22. Cermàkovà I et al. (2010) Grade III lipaemia retinalis in a newborn. Acta Ophthalmol, 88: e141-2.

23. Lu CK et al. (2005) Electrophysiological changes in lipaemia retinalis. Am J Ophthalmol, 139: 1142-5.

24. Jain A et al (2017) Lipemia retinalis in an infant treated for retinopathy of prematurity. J aapos, 21: 254-7.

25. Yamamoto H et al. (2014) Autoimmune severe hypertriglyceridemia induced by anti-apolipoprotein C-II antibody. J Clin Endocrinol Metab, 99: 1525-30.

26. Leipert G (1995) [Fatty aqueous humor and transient retinal lipemia in a case of Sheehan's disease]. Klin Monbl Augenheilkd Augenarztl Fortbild, 127: 558-65.

27. Everett WG (1952) Nondiabetic lipemia retinalis; report of a case. AMA Arch Ophthalmol, 48: 712-5.

28. Wetzel B et al. (2021) Lipemia Retinalis During Chemotherapy With Adjunctive Glucocorticoid Treatment In A Patient With Colon Carcinoma. Retin Cases Brief Rep, 15: 450-2.

29. Abramson DH et al. (1995) Steroid and asparaginase-induced hyperlipidemia in leukemia. Insight, 20: 12-3.

30. Eng KT et al. (2000) Lipemia retinalis in acquired immunodeficiency syndrome treated with protease inhibitors. Archives of Ophthalmology, 118: 425-6.

31. Nampoothiri S et al. (2011) Lipoprotein lipase deficiency in an infant. Indian Pediatr, 48: 805-6.