To cite this article: Gok G, Bal C, Akbulut ED, Uzdogan A, Yilmaz G, Erel O. The three years' experience of long and very long chain fatty acid analysis. Turk J Clin Lab 2024; 3: 358-363

Research Article

The three years' experience of long and very long chain fatty acid analysis

Uzun ve çok uzun zincirli yağ asit analizinde üç yıllık deneyim

Gamze Gok*[1], Ceylan Bal[1,2], Emis Deniz Akbulut[1], Andac Uzdogan[1], Gulsen Yilmaz[1,2], Ozcan Erel[1,2]

[1]Health Ministry Of Turkey Republic Ankara Bilkent City Hospital, Medical Biochemistry Laboratory, Ankara, Turkey,

[2]Ankara Yıldırım Beyazıt University, Faculty of Medicine, Department of Medical Biochemistry, Ankara, Turkey.

Abstract

Aim: Cellular lipids, such as cholesterol esters, sphingolipids, and glycerolipids contain Fatty acids (FAs). FAs take place in many living structures and FAs are useable for diagnosing and examining some diseases. FAs including 22 or more carbon atoms are defined as very long-chain fatty acids (VLCFAs). This study aimed to evaluate Ankara Bilkent City Hospital's results of VLCFA analysis data and present contributions to the literature.

Material and Methods: The present study involved a total of 5973 C22:0, 5973 C24:0, 5973 C26:0, 5664 phytanic acid, and 5658 pristanic acid analysis results, and 5973 C24/C22 and, 5658 C26/C22 ratios. The VLCFA analysis was performed by the SHIMADZU Gas Chromatograph Mass Spectrometer (GCMS) QP2010 SE system with the Eureka and the Obikrom kits. The analysis results between 01/01/2020 and 31/12/2022 in Ankara Bilkent City Hospital Biochemistry Laboratory were involved.

Results: The positive results were as follows; 207 (%3.5) for C22:0, 149 (%2.5) for C24:0, 340 (%5.7) for C24:0/C22:0 ratio, 111 (%1.9) for C26:0, 158 (%2.9) for C26:0/C22:0 ratio, 89 (%1.6) for Phytanic Acid, and 8 (%0.1) for Pristanic Acid. The male group had a higher number of positive results for C22:0 ($p<0.019$) and C24:0/C22:0 ratio ($p<0.001$). The pediatric group had a higher number of positive results for C26:0/C22:0 ($p=0.032$).

Conclusion: We shared our three-year LCFA and VLCFA analysis experience with this study. We also evaluated the analysis results according to gender and age groups. The present study may be helpful for future investigations.

Keywords: Very Long Chain Fatty Acids; Gas Chromatography-Mass Spectrometry; Peroxisomal Disorders

Corresponding Author*: Gamze Gok, Health Ministry Of Turkey Republic Ankara Bilkent City Hospital, Medical Biochemistry Laboratory, Ankara, Türkiye
E-mail: gamze_gok@outlook.com
Orcid: 0000-0002-2804-5548
Doi: 10.18663/tjcl.1458978
Recevied: 27.03.2024 accepted: 08.07.2024

TJCL Volume 15 Number 3 p: 358-363

Öz

Amaç: Kolesterol esterleri, sfingolipidler ve gliserolipitler gibi hücresel lipitler, Yağ asitleri (YA) içerir. YA'lar birçok canlı yapıda yer almakta ve YA'lar bazı hastalıkların teşhisinde ve incelenmesinde kullanılmaktadır. 22 veya daha fazla karbon atomu içeren YA'lar çok uzun zincirli yağ asitleri (ÇUZYA'lar) olarak tanımlanır. Bu çalışmada Ankara Bilkent Şehir Hastanesi'nin ÇUZYA analiz verilerinin sonuçlarının değerlendirilmesi ve literatüre katkı sunulması amaçlandı.

Gereç ve Yöntemler: Bu çalışmaya toplam 5973 C22:0, 5973 C24:0, 5973 C26:0, 5664 fitanik asit ve 5658 pristanik asit analiz sonucu ile 5973 C24/C22 ve 5658 C26/C22 oranları dahil edildi. VLCFA analizi, Eureka ve Obikrom kitleri ile SHIMADZU Gaz Kromatograf Kütle Spektrometresi (GCMS) QP2010 SE sisteminde gerçekleştirildi. Ankara Bilkent Şehir Hastanesi Biyokimya Laboratuvarında 01/01/2020 ile 31/12/2022 tarihleri arasında yapılan analiz sonuçları dahil edildi.

Bulgular: Pozitif sonuçlar; C22:0 için 207 (%3.5), C24:0 için 149 (%2.5), C24:0/C22:0 oranı için 340 (%5.7), C26:0 için 111 (%1.9), 158 (%2.9) C26:0/C22:0 oranı için, Fitanik Asit için 89 (%1.6) ve Pristanik Asit için 8 (%0.1) idi. Erkek grupta C22:0 ($p<0,019$) ve C24:0/C22:0 oranı ($p<0,001$) açısından daha yüksek sayıda pozitif sonuç elde edildi. Pediatrik grupta C26:0/C22:0 için daha yüksek sayıda pozitif sonuç vardı ($p=0,032$).

Sonuç: Üç yıllık UZYA ve ÇUZYA analiz deneyimimizi bu çalışmayla paylaştık. Analiz sonuçlarını cinsiyet ve yaş gruplarına göre de değerlendirdik. Bu çalışma gelecekte yapılacak araştırmalara yardımcı olabilir.

Anahtar Kelimeler: Çok Uzun Zincirli Yağ Asitleri; Gaz Kromatografisi-Kütle Spektrometresi; Peroksizomal Bozukluklar

Introduction

Fatty acids (FAs) are a component of almost every cell [1]. FAs are the building blocks of fats [2]. Cellular lipids, such as cholesterol esters, sphingolipids, and glycerolipids contain FAs [3]. FA molecules are parts of membrane lipids, with varying numbers of double bonds, chain lengths, and hydroxylation positions [4]. The number of carbons in fatty acids varies between 2 and 34, and with the difference in carbon numbers, fatty acids can be classified according to the number of carbons they contain. Fatty acids with less than six carbon numbers are classified as short-chain fatty acids, fatty acids with six to ten carbon numbers are classified as medium-chain fatty acids, and fatty acids with more than ten carbon numbers are classified as long-chain fatty acids (LCFAs) [2]. FAs with 22 or more carbon atoms are very long-chain fatty acids (VLCFAs) [4]. Each VLCFA presents specific functions. They take part in the maintenance of myelin, formation of the skin barrier, spermatogenesis, anti-inflammation, retinal function, and liver homeostasis. VLCFAs do not independently obtain these functions [3]. VLCFAs can be synthesized from normal chain fatty acids by the elongation reaction in the endoplasmic reticulum. VLCFAs, which are activated by coenzyme A and become VLCFA-CoA, are transferred to the peroxisome. VLCFAs are shortened in the peroxisome and become ready for mitochondrial oxidation [5]. In mammals, VLCFAs are degraded by peroxisomal oxidation. With peroxisomal oxidation, the chain lengths of fatty acids are shortened and they become ready for mitochondrial beta-oxidation transfer [6]. Peroxisomal enzymes act on VLCFAs [7]. Being part of many living structures, from microscopic to macroscopic, makes fatty acids useable for diagnosing and examining some diseases [8]. In the human body, several diseases may occur due to impaired VLCFA metabolism [9]. X-linked adrenoleukodystrophy (X-ALD), childhood-onset cerebral adrenoleukodystrophy (CCALD), and adrenomyeloneuropathy (AMN) are some forms of related diseases [4].

In Ankara Bilkent City Hospital's medical biochemistry laboratory, FAs with 22 Carbon atoms (C22:0), with 24 Carbon atoms (C24:0), with 26 Carbon atoms (C26:0), and phytanic acid, and pristanic acid analyses are performed with the SHIMADZU Gas Chromatograph Mass Spectrometer (GCMS) QP2010 SE device. Furthermore, if requested by the clinicians C24/C22 and C26/C22 ratios are calculated and presented in the patient result reports. The purpose of this retrospective study, which includes LCFA and VLCFA analysis data conducted at Ankara Bilkent City Hospital between 01.01.2020 and 31.12.2022, is to contribute to the literature.

Material And Methods

A total of 5973 C22:0, 5973 C24:0, 5973 C26:0, 5664 phytanic acid, and 5658 pristanic acid analysis results, and 5973 C24:0/C22:0 and 5658 C26:0/C22:0 ratios were included in this study. LCFA and VLCFA analyses were performed by the SHIMADZU Gas Chromatograph Mass Spectrometer (GCMS) QP2010 SE system with the Eureka Fatty Acids in Plasma By GC/MS kit (Code GC75010) (Eureka S.R.L. Lab Division Direzione e

Coordinamento Sentinel CH. Spa) and the Obikrom VLCFA GCMS (KK.53/01.07.2021/Rev.00) (Obikrom Analysis and Laboratory Services Inc./Türkiye)

The Eureka Fatty Acids in Plasma By GC/MS kit (Code GC75010) (Eureka S.R.L. Lab Division Direzione E Coordinamento Sentinel Ch. Spa) contains three reagents, and these are Raegent A, Reagent B, and Reagent C. The procedure was as follows. 3ml of whole blood was taken to EDTA containing sample tube and centrifuged at 4000 rpm for 5 minutes. 100 µl plasma and 100 µl Reagent A were poured into a suitable glass tube and vortexed for 60 seconds and added 2ml of Acetonitril-HCL solution (The solution includes 8 ml acetonitrile + 2 ml 10M HCl) and vortexed for 60 seconds. Tubes were put at 110 °C for 46 minutes and during this time shaken every 15 minutes then cooled down at room temperature. 5 ml n-Hexane was added and vortexed for 60 seconds, 0,5 ml 10M HCl was added and vortexed for seconds, and centrifuged at 4000 rpm for 5 minutes. The supernatant was taken and transferred to a clean tube of 15 ml. 4 ml KOH solution (The solution was made up of 5,6 gr KOH+ 100ml ultrapure water.) was added, vortexed for 60 seconds, and centrifuged at 4000 rpm for 5 minutes. The supernatant was taken and transferred to a clean tube of 10ml and evaporated to dryness. After drying 50 µl Reagent B was added, vortexed for 60 seconds, and evaporated to dryness. After drying 50 µl M-BSTFA and 50 µl Reagent C were added, vortexed for 60 seconds, incubated at 65˚C for 35 minutes (min), cooled down to room temperature, and finally 1 l volume was injected into the GCMS system.

The Obikrom VLCFA GCMS kit (KK.53/01.07.2021/Rev.00) (Obikrom Analysis and Laboratory Services Inc./Türkiye) contains three reagents, Reagent A, Reagent B, and Reagent C. 100 µl plasma and 100 µl Reagent A were poured into a suitable glass tube and vortexed for 1 min and added 2ml of Acetonitril-HCL solution (The solution includes 4 ml acetonitrile and 1 ml 10M HCl.) and vortexed for 1 minute. Tubes were put at 110 °C for 46 minutes and during this time shaken every 15 minutes then cooled down at room temperature. 2ml of NaOH solution (The solution was made up of 2 gr NaOH, 1 ml distilled water, and 49 ml Methanol.) was added, vortexed for 1 minute, and incubated at 110 °C for 46 minutes and during this time vortexed every 15 minutes, cooled down to room temperature. 5 ml hexane was added to the tubes, and vortexed for 1 minute, 500 µl of 10M HCl was added, vortexed for 1 minute, and centrifuged at 4000 rpm for 5 minutes. After centrifugation, the upper phase is transferred to clean conical falcon tubes and 4 ml KOH solution is added to the tubes, vortexed for 1 minute, and centrifuged at 4000 rpm for 5 minutes. After centrifugation, the upper phase was discarded and the middle phase and lower phase were kept. 5 ml of hexane

was added to the tubes, and vortexed for 1 minute. 500 µl 10M HCl was, vortexed for 1 minute and centrifuged at 4000RPM for 5 minutes. After centrifugation, the upper phase was transferred to clean glass tubes. Samples were allowed to evaporate. After the evaporation process, 50 µl Reagent B was added, then vortexed for 1 minute, and evaporated. After the evaporation process 50ul MBSTFA and Reagent C were added, vortexed for 1 minute incubated at 65 ˚C for 35 minutes, and cooled down to room temperature. Finally, it was taken into an insert vial and injected into the GCMS device.

During the analysis, TRB 5MS 30mx0,25mmx1um column was used. The injection temperature was 280 ˚C, the split ratio was 10, Column Temperature was 120˚C x1 min and 20 ˚C/min up to 300 ˚C. The analysis was conducted in 38 minutes and the flow of the Helium gas was 1ml/min. MS temperature was 230 ˚C, interface temperature was 280 ˚C, the scan type was SIM, and the ions were as follows; pristanic IS (internal standard) 358.00, pristanic 355.00, phytanic IS 372.00, phytanic 369.00, C22 IS 401.00, C22 397.00, C24 IS 429.00, C24 425.00, C26 IS 457.00, C26 453.00.

Our hospital's laboratory information system includes disease diagnoses according to the International Disease Classification Codes. In the present retrospective study, the data of patients who underwent LCFA and VLCFA analysis in the Medical Biochemistry Laboratory of Ankara Bilkent City Hospital between 01/01/2020 and 31/12/2022 were evaluated by obtaining them from the hospital information system.

Our study involved a single result for each patient, and only the first result of patients who had fatty acid analysis multiple times was included. Ethics approval was acquired from Ankara Bilkent City Hospital's Ethic Committee for this study. (E1-23-3808). The researchers worked under the Declaration of Helsinki at every stage of the present study. In the present study, no informed consent was obtained from the patients.

Statistical Analysis

The data of descriptive statistics were enunciated as numerically, mean, median, and interquartile ranges (IQR), and categorical variables were enunciated as percentages. A chi-square test was used in the groups' categorical data comparison. A p-value <0.05 was accepted as statistically significant. IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA) was utilized for the Statistical analyses. Microsoft Excel 2021 was used for graphs.

Results

The present study involved a total of 5973 C22:0, 5973 C24:0, 5973 C26:0, 5664 phytanic acid, and 5658 pristanic acid analysis results, and 5973 C24/C22 and, 5658 C26/C22 ratios.

Each data was separately evaluated according to pediatric (0-18 years), adult (0-64 years), and geriatric (65 years and over) age groups and gender groups. The distribution of age groups is presented (Table 1).

The minimum analysis result values expressed to be considered as positive used in the analysis were the higher values of 90.3 µmol/L for C22:0, 79.4 µmol/L for C24:0, 1.3 µmol/L for C26:0, for 3.77 µmol/L Phytanic Acid, and1.5 µmol/L for Pristanic Acid. The minimum ratio values expressed as to be considered positive were the higher values of 1.008 for C24/C22 and 0.026 for C26/C22. LCFA and VLCFA test analysis data are presented (Table 2). LCFA and VLCFA test analysis data among genders (Table 3) and among age groups (Table 4) are presented. Percentages of Test Analysis Data Among Age Groups (Graph 1) and Test Analysis Data Among Genders (Graph 2) are presented.

Table 1. Distribution of Age Groups

	Pediatric Group	Adult Group	Geriatric Group	p*
C22:0 (µmol/L)	4 [3-9]	20 [19-41.5]	69.5 [65-74.5]	<.001
C24:0 (µmol/L)	4 [3-9]	20 [19-44]	67 [65-73.5]	<.001
C24:0/C22:0	4 [3-9]	20 [19-41.5]	69.5 [65-74.5]	<.001
C26:0 (µmol/L)	4 [3-9]	20 [19-41.5]	69.5 [65-74.5]	<.001
C26:0/C22:0	4 [2-9]	20 [19-42]	69.5 [65-74.5]	<.001
Phytanic Acid(µmol/L)	4 [3-9]	20 [19-21.75]	73 [68-None]	<.001
Pristanic Acid (µmol/L)	4 [3-9]	20 [19-21]	73 [68-None]	<.001

The data are presented with the median and interquartile ranges (IQR) of the groups.
p*: Kruskal Wallis Test

Table 2. Long and Very Long Chain Fatty Acid Test Analysis Data

	Negative N (%)	Positive N (%)
C22:0 (µmol/L)	5766 (96.5)	207 (3.5)
C24:0 (µmol/L)	5824 (97.5)	149 (2.5)
C24:0/C22:0	5633 (94.3)	340 (5.7)
C26:0 (µmol/L)	5862 (98.1)	111 (1.9)
C26:0/C22:0	5299 (97.1)	158 (2.9)
Phytanic Acid (µmol/L)	5575 (98.4)	89 (1.6)
Pristanic Acid (µmol/L)	5650 (99.9)	8 (0.1)

N: Number of the population

Table 3. Long and Very Long Chain Fatty Acid Test Analysis Data Among Genders

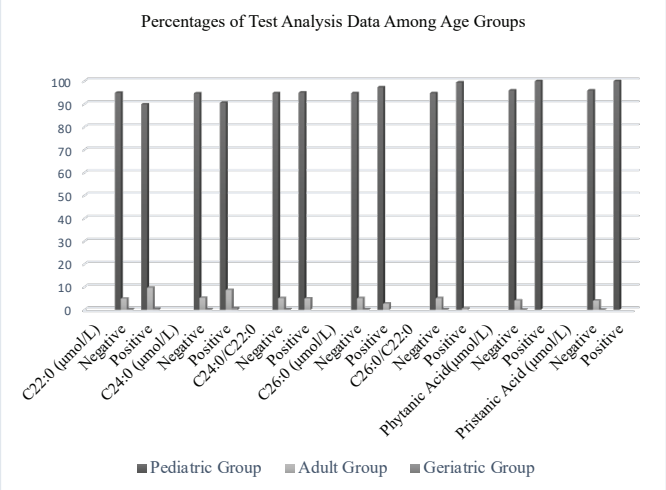
	Female	Male	
	N (%)	N (%)	p*
C22:0 (µmol/L)			
Negative	2342 (40.6)	3424 (59.4)	0.019
Positive	101 (48.8)	106 (52.2)	
C24:0 (µmol/L)			
Negative	2375 (40.8)	3449 (59.2)	0.238
Positive	68 (45.6)	81 (54.4)	
C24:0/C22:0			
Negative	2347 (41.7)	3286 (58.3)	<0.001
Positive	96 (38.2)	244 (71.8)	
C26:0 (µmol/L)			
Negative	2389 (40.8)	3473 (59.2)	0.098
Positive	54 (48.6)	57 (51.4)	
C26:0/C22:0			
Negative	2157 (40.7)	3142 (59.3)	0.219
Positive	72 (45.6)	86 (54.4)	
Phytanic Acid(µmol/L)			
Negative	2243 (40.2)	3332 (59.8)	0.587
Positive	33 (37.1)	56 (62.9)	
Pristanic Acid (µmol/L)			
Negative	2269 (40.2)	3381 (59.8)	0.722
Positive	4 (50)	4 (50)	

p*: Chi-square Test, N: Number of the population

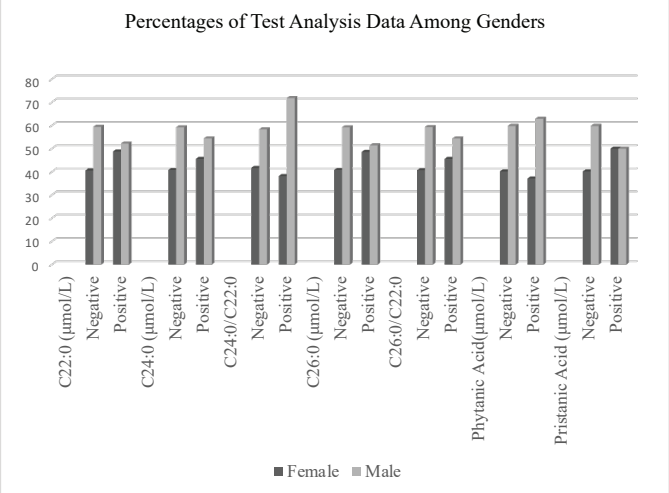
Table 4. Long and Very Long Chain Fatty Acid Test Analysis Data Among Age Groups

	Pediatric Group	Adult Group	Geriatric Group	
	N (%)	N (%)	N (%)	p*
C22:0 (µmol/L)				
Negative	5473 (94.9)	280 (4.9)	13 (0.2)	0.06
Positive	186 (89.9)	20 (9.7)	1 (0.5)	
C24:0 (µmol/L)				
Negative	5509 (94.6)	302 (5.2)	13 (0.2)	0.85
Positive	135 (90.6)	13 (8.7)	1 (0.7)	
C24:0/C22:0				
Negative	5336 (94.7)	283 (5.0)	14 (0.2)	0.654
Positive	323 (95)	17 (5)		
C26:0 (µmol/L)				
Negative	5551 (94.7)	297 (5.1)	14 (0.2)	0.46
Positive	108 (97.3)	3 (2.7)		
C26:0/C22:0				
Negative	5017 (94.7)	272 (5.1)	10 (0.2)	0.032
Positive	157 (99.4)	1 (0.6)		
Phytanic Acid(µmol/L)				
Negative	5344 (95.9)	228 (4.1)	3 (0.1)	0.146
Positive	89 (100)			
Pristanic Acid (µmol/L)				
Negative	5420 (95.9)	227 (4)	3 (0.1)	0.844
Positive	8 (100)			

p*: Chi-square Test, N: Number of the population



Graph 1: Percentages of Test Analysis Data Among Age Groups



Graph 2: Percentages of Test Analysis Data Among Genders

The diagnoses of patients whose results are evaluated as positive in the laboratory information system were as follows; certain infectious and parasitic diseases, neoplasms, diseases of the blood and blood-forming organs, and certain disorders involving the immune mechanism, endocrine, nutritional, and metabolic diseases, mental and behavioral disorders, diseases of the nervous system, diseases of the eye and adnexa, diseases of the circulatory system, diseases of the respiratory system, diseases of the digestive system, diseases of the skin and subcutaneous tissue, diseases of the skin and subcutaneous tissue, diseases of the musculoskeletal system and connective tissue, diseases of the genitourinary system, certain conditions originating in the perinatal period, congenital malformations, deformations and chromosomal abnormalities, symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified, factors influencing health status and contact with health services. As stated, the diagnoses of patients with positive analysis results varied.

Discussion

Plasma VLCFAs, C26:0/C22:0 ratio; phytanic and pristanic acids, and pristanic/phytanic acid ratio are some of the diagnostic tests in peroxisomal disorders [10]. Refsum disease, (both infantile and classic), Zellweger syndrome, Neonatal adrenoleukodystrophy, and Rhizomelic chondrodysplasia punctata are the common peroxisomal biogenesis disorders [11].

Elevated levels of plasma phytanic acid are essential for Refsum Disease [12]. In Refsum disease, plasma phytanic acid level is >200 µmol/L. This finding is pathognomic for Refsum disease [11]. In Zellweger syndrome, peroxisomal biogenesis is completely defective, and increased VLCFA, pristanic acid, and phytanic acid are observed in the plasma [12]. X-ALD which is the world's most common peroxisomal disorder is caused by mutations in the ABCD1 gene [13]. Peroxisomes's beta-oxidation impairment causes VLCFA accumulation in blood and some varied tissues [14]. Accumulated VLCFA values in the blood, high levels of C26:0, and high ratios of C24:0/C22:0 and C26:0/C22:0 are used for the diagnosis purposes of X-ALD. Rattay et al. examined the VLCFA results of 1908 patients in their study and stated that 45 cases were above the cut-off value. The X-ALD positivity of these patients was confirmed by ABCD1 gene mutation genetic testing. Of the 45 patients with high VLCFA values, 30 were found to be X-ALD positive and 15 were negative. [13]. In the present study, we evaluated a total of 5973 C22:0, 5973 C24:0, 5973 C26:0, 5664 phytanic acid, and 5658 pristanic acid analysis results, and 5973 C24/C22 and, 5658 C26/C22 ratios. The positive results were as follows; 207 (%3.5) for C22:0, 149 (%2.5) for C24:0, 340 (%5.7) for C24:0/C22:0 ratio, 111 (%1.9) for C26:0, 158 (%2.9) for C26:0/C22:0 ratio, 89 (%1.6) for Phytanic Acid, and 8 (%0.1) for Pristanic Acid (Table 2).

Abnormal lipid metabolism and abnormalities in peroxisome metabolism can be observed during the pathogenesis of osteoarthritis. Peroxisomal dysfunction may lead to the accumulation of VLCFAs and LCFAs in osteoarthritis patients [15].

Chu et al.; stated -in their study investigating the relationship between VLCFA and cancer- that decreased VLCFA levels were associated with slow growth of tumor cells and that VLCFA elongation was necessary for the growth of tumor cells [16].

Lipids also have functions in the nervous system. They play a role

in synapse stabilization, signal transmission and homeostatic balance of signaling molecules, protection of neurons and regulation of DNA, and inflammation responses. It has been stated that fatty acids may play a role in different stages of some retinal disease processes such as diabetic retinopathy, age-related macular degeneration, and retinitis pigmentosa. Very long-chain polyunsaturated fatty acids are depleted in diabetic retinopathy and age-related macular degeneration [17].

The patients we evaluated as positive in our study had diagnoses other than metabolic diseases that we obtained from the laboratory information system. Similar to our study, it has been reported in the literature that VLCFA levels are elevated in different kinds of diseases [15, 16, 17].

To the best of our knowledge, this is the first study presenting the LCFA and VLCFA analysis data of three years, comparing the groups according to gender and age, and evaluating the results by laboratory specialists. The data was sourced from one of Türkiye's largest laboratories, and fatty acid analyses are routinely conducted at our hospital.

The strength of our study is as follows: The data included in the present study covers 3 years; all data are evaluated in different age groups and genders. The limitations of our study are as follows: the data we obtained were evaluated only by laboratory experts and no clinical information nor genetic analysis results were involved, and we could not get information about the special diets, treatments, and medications of the people who underwent VLCFA and LCFA analyses, if any. It would be useful to conduct future studies that include detailed patient data.

Conclusion

We shared our three-year LCFA and VLCFA analysis experience with this study. We also evaluated the analysis results according to gender and age groups. We think the present study may be helpful for future investigations.

Conflict of interest

No person/organization financially supports the study and the authors have no conflict of interest.

References

1. Kyselová, L., M. Vítová, and T. Řezanka, Very long chain fatty acids. Progress in Lipid Research, 2022: p. 101180.
2. Marten, B., M. Pfeuffer, and J. Schrezenmeir, Medium-chain triglycerides. International Dairy Journal, 2006. 16(11): p. 1374-1382.
3. Kihara, A., Very long-chain fatty acids: elongation, physiology and related disorders. The journal of biochemistry, 2012. 152(5): p. 387-395.
4. Erdbrügger, P. and F. Fröhlich, The role of very long chain fatty acids in yeast physiology and human diseases. Biological chemistry, 2020. 402(1): p. 25-38.
5. Sassa, T. and A. Kihara, Metabolism of very long-chain fatty acids: genes and pathophysiology. Biomolecules & therapeutics, 2014. 22(2): p. 83.
6. Poirier, Y., et al., Peroxisomal β-oxidation—a metabolic pathway with multiple functions. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research, 2006. 1763(12): p. 1413-1426.
7. Masters, C.J. and D.I. Crane, On the role of the peroxisome in ontogeny, ageing and degenerative disease. Mechanisms of ageing and development, 1995. 80(2): p. 69-83.
8. De Carvalho, C.C. and M.J. Caramujo, The various roles of fatty acids. Molecules, 2018. 23(10): p. 2583.
9. Moser, H.W. and A.B. Moser, Very long-chain fatty acids in diagnosis, pathogenesis, and therapy of peroxisomal disorders. Lipids, 1996. 31(1Part2): p. S141-S144.
10. Baumgartner, M.R. and J.M. Saudubray. Peroxisomal disorders. in Seminars in neonatology. 2002. Elsevier.
11. Kumar, R. and O. De Jesus, Refsum disease. 2020.
12. OKUR, İ., Peroksizomal Bozukluklar. 2017.
13. Rattay, T.W., et al., Defining diagnostic cutoffs in neurological patients for serum very long chain fatty acids (VLCFA) in genetically confirmed X-Adrenoleukodystrophy. Scientific reports, 2020. 10(1): p. 15093.
14. Chaudhry, V., H.W. Moser, and D.R. Cornblath, Nerve conduction studies in adrenomyeloneuropathy. Journal of Neurology, Neurosurgery & Psychiatry, 1996. 61(2): p. 181-185.
15. Song, J., et al., HIF-1α: CRAT: miR-144-3p axis dysregulation promotes osteoarthritis chondrocyte apoptosis and VLCFA accumulation. Oncotarget, 2017. 8(41): p. 69351.
16. Chu, Q., et al., Stearate-derived very long-chain fatty acids are indispensable to tumor growth. The EMBO journal, 2023. 42(2): p. e111268.
17. Nwagbo, U. and P.S. Bernstein, Understanding the roles of very-long-chain polyunsaturated fatty acids (VLC-PUFAs) in eye health. Nutrients, 2023. 15(14): p. 3096.