Section: Biochemistry

Research

ALZHEIMER'S DISEASE: EARLY AND SPECIFIC DIAGNOSIS BY PLASMA LIPIDOMICS APPROACH

Leena Chacko[1], Madhava Rao Veeramalla[2], Chandrasekhar Valupadas[3], Hari Prasad Reddy Paluru[4], Ramesh Kandimalla[5]

[1]BioAnalytical Lab, Meso Scale Discovery, 1601 Research Blvd, Rockville, MD, USA.
[2]Associate Professor (In charge HOD), Department of Neurology, Govt. Medical College, Mahabubabad, Telangana, India.
[3]Medical Superintendent & Professor of General Medicine, MGM Hospital, Warangal, Telangana, India.
[4]Department of Bio-Technology, Sri Krishnadevaraya University, Anantapur, India.
[5]Assistant Professor, Department of Biochemistry, Kakatiya Medical College, Warangal, Telangana, India.

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Corresponding Author:
Dr. Ramesh Kandimalla,
Email: ramesh.kandimalla@gmail.com
ORCID: 0000-0002-3313-4393

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Abstract

Background: Identification of early AD alterations and the discovery of novel potential biomarkers may be aided by the analysis of lipid profiles in plasma samples. to assess the relative importance of lipid metabolism dysfunction and pathophysiology pathway in Alzheimer's disease. **Materials and Methods:** The study included 66 people of which 10 had preclinical Alzheimer's disease, 35 had mild cognitive impairment AD and 21 were healthy. Their plasma samples were subjected to an untargeted lipidomic analysis. To pinpoint variables and analyse the profile of lipid families, two complementary techniques were chosen. Later, a focused examination was done for a few of the discovered lipids. **Result:** Diglycerol, Lys phosphatidylethanolamine, Lys phosphatidylcholine, monoglyceride, and sphingomyelin families of lipids, as well as monounsaturated lipids, were shown to differ statistically significantly among the participant groups. Statistically significant variations in the levels of DG, MG, and PE seen between the MCI-AD and healthy groups, whereas differences in the levels of ceramides (Cer), LPE, LPC, MG, and SM were seen between the preclinical AD and healthy groups. Additionally, the targeted study between early AD (preclinical and MCI) and healthy subjects revealed statistically significant changes in 18:1 LPE. **Conclusion:** The various plasma lipid profiles may aid in the early and non-invasive detection of AD. Among the lipid families, DGs, LPEs, LPCs, MGs, and SMs produced pertinent data. Particularly, MGs might be helpful in detecting AD, whereas LPEs, LPCs, and SM appear to be more associated with the preclinical stage, and DGs are more associated with the MCI stage. In particular, 18:1 LPE shown potential use as an AD biomarker.

INTRODUCTION

The most frequent cause of dementia, accounting for around 70% of all cases, is Alzheimer's disease (AD). This neurodegenerative condition that worsens over time has a sneaky onset and is clinically identified by memory loss that worsens over time along with other cognitive abnormalities.[1,2] One of the biggest problems facing the economic and public health systems of the twenty-first century is AD. On the genesis of this complex disease, which includes proteinopathies as well as oxidative stress, inflammation, metabolic imbalance, and other variables, there is currently no international agreement. The significance of discovering early biomarkers for AD diagnosis is highlighted by the lack of effective treatments and the possibility of prevention.[2,3] Furthermore, it has been shown that AD-related degenerative processes might also present in the peripheral system,[4,5] suggesting the potential for discovering non-invasive blood biomarkers. Lipids serve as crucial signalling molecules and take part in processes like the development of cell membranes, cellular transport, and energy storage. In addition to their structural functions, lipids have also been demonstrated to modulate transmembrane proteins like ion channels. This means that changing the composition or conformation of the lipids around ion channels can change how well those channels work. Blood lipids have become prospective biomarkers for AD because of the vital role lipids play in many important biological processes.[3,4]

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There have been few investigations on the plasma lipidome in AD, despite the large number of publications on the relationship between lipids and the pathobiology of AD. Lipidomics techniques concurrently identify and measure hundreds of lipids, in contrast to traditional biochemical approaches that concentrate on individual metabolites or processes.[5,6] Large-scale lipid measurements enable network analysis techniques and give access to ways to pinpoint crucial metabolic factors in disease pathogenesis. Powerful techniques for mapping global biochemical changes in illness and treatment are provided by lipidomics.[7]

This paper assesses plasma lipid profiles using untargeted and targeted methods to identify lipid families and specific lipids involved in early AD as potential biomarkers.

MATERIALS AND METHODS

The study was performed at PGIMER, Chandighar from 2007-2010. The participants ranged in age from 50 to 80 who were divided into three groups: individuals with preclinical Alzheimer's disease (n = 10), people with mild cognitive impairment (MCI) caused by AD (n = 35), and those in healthy controls (n = 21). The clinical evaluation included a neuropsychological assessment based on the Mini-Mental State Examination (MMSE), Functionality Assessment Questionnaire (FAQ), Repeatable Battery for Assessment of Neuropsychological Status Delayed Memory (RBANS.DM), and Clinical Dementia Rating (CDR). Additionally, studies of the cerebrospinal fluid (CSF) (-amyloid-42 peptide, total Tau, and phosphorylated Tau) and NMR-TAC were performed.

Methodology

Participants' blood was drawn, centrifuged to separate the plasma components, and then kept at 80 C pending analysis. Pea-Bautista et al. previously detailed the plasma sample treatment; In a nutshell, 50 litres of plasma were mixed with 150 litres of cold isopropanol (IPA), vortexed, and maintained at 20 °C for 30 minutes. 90 L of the supernatant was then added to a 96-well plate after it had been centrifuged (13,000 g, 10 min, 4 °C). Then, each sample received 10 L of an internal standard (IS) mix solution composed of 100 g/mL each of three different compounds: 17:0 LPC, d18:1/17:0 SM, and 17:0 PE. Ten millilitres (L) of each plasma sample were combined to create the quality control (QC). The same extraction tube used for blood collection was utilised to prepare a blank with ultrapure water. Additionally, time-of-flight mass spectrometry and ultra-performance liquid chromatography were used to evaluate the samples. Both untargeted and targeted analysis were carried out.[7,8]

Inclusion Criteria

- Patients between age 50-80 years
- Patients of either sex

Exclusion Criteria

- Patients with serious neurological or psychological disorders.
- Patients above age 80 and below age 50

RESULTS

The individuals' clinical and demographic features are outlined. As anticipated, there were statistically significant differences between the participant groups for the neuropsychological measures (CDR, RBANS, FAQ, and MMSE) and the CSF biomarkers (amyloid 42, t-Tau, and p-Tau). Additionally, there were statistically significant differences in age between the groups. In this regard, the relationships between age and all lipids (from the untargeted and targeted analyses) were evaluated, however no lipid showed any significant results.

Table 1: Clinical and demographic participant characteristics

		Healthy (n = 21)	MCI-AD (n = 35)	Preclinical AD (n = 10)	p Value (Kruskal–Wallis)
Median Age (years) (IQR)		61 (58, 68)	70 (69, 74)	68 (60, 74)	0.000
Gender (Female, n (%))		15 (71%)	9 (25%)	7 (70%)	0.737
Educational Level	Primary (n (%)) Secondary (n (%))	7 (34%) 4(19%)	10(28%) 15(43%)	4 (40%) 2 (20%)	0.023
	University (n (%))	10(47%)	10(29%)	4 (40%)	
Concomitant Medication	Statins (n (%)) Fibrates (n (%)) Benzodiazepines (n (%)) Antidepressants (n (%)) Antiepileptics (n (%))	9(41%) 0 (0%) 6(27%) 7(32%) 1 (5%)	12 (63%) 3 (17%) 3 (16%) 2 (11%) 0 (0%)	3(25%) 1 (8%) 2 (17%) 0 (0%) 0 (0%)	0.335 0.143 0.635 0.085 0.547
	Antihypertensives (n (%))	7(32%)	9 (50%)	2 (29%)	0.424
	Corticoids (n (%))	1 (5%)	0 (0%)	0 (0%)	0.547
	Anti-inflammatories (n (%))	3 (14%)	0 (0%)	0 (0%)	0.151
Comorbidities	Dyslipidemia (n (%)) Diabetes (n (%)) Hypertension (n (%))	11 (50%) 3 (14%) 8 (36%)	11 (58%) 2 (11%) 9 (47%)	3(43%) 0 (0%) 2 (29%)	0.766 0.589 0.628
	Heart Disease (n (%))	1 (5%)	0 (0%)	0 (0%)	0.547
	Cerebrovascular (n (%))	1 (5%)	0 (0%)	0 (0%)	0.547

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Smoke (Yes, n (%))	6 (27%)	3 (16%)	1 (14%)	0.598
Alcohol (Yes, n (%))	6 (27%)	2 (11%)	0 (0%)	0.157
Depression (Yes, n (%))	5 (23%)	5 (26%)	2 (29%)	0.939
Anxiety (Yes, n (%))	4 (18%)	3 (16%)	2 (29%)	0.757
Amyloid β42 (pg mL−1) Median (IQR)	1224 (964, 1421)	495 (452, 622)	572 (383, 694)	0.000
t-Tau (pg mL−1) Median (IQR)	212 (181, 259)	578 (449, 793)	444 (208, 611)	0.000
p-Tau (pg mL−1) Median (IQR)	34 (25, 39)	91 (62, 109)	74 (28, 94)	0.000
CDR Median (IQR)	0.5 (0, 0.5)	0.5 (0.5, 0.5)	0.5 (0, 0.5)	0.001
MMSE Median (IQR)	29 (28, 29)	24 (22, 25)	29 (27, 30)	0.000
RBANS.DM Median (IQR)	98 (94, 103)	42 (40, 53)	95 (87, 101)	0.000
FAQ Median (IQR)	1 (0, 4)	7 (5, 10)	1 (0, 3)	0.000

Table 2: Average sum of the different lipid families' levels in the participant groups (preclinical AD, MCI-AD, and healthy).

Lipid Family	Healthy Controls (HC) (n = 21)	MCI-AD (n = 35)	Preclinical AD (n = 10)	p Value (Kruskal–Wallis)	Healthy vs. Preclinical AD (Mann–Whitney, p Value)	Healthy vs. MCI-AD (Mann–Whitney, p Value)
CE (a.u.)	4.15 (2.86, 4.83)	3.60 (3.03, 5.04)	4.47 (3.86, 4.96)	0.415	0.349	0.685
Cer (a.u.)	4.39 (3.52, 4.39)	3.94 (2.42, 5.75)	5.67 (5.09, 6.87)	0.070	0.038 *	0.452
DG (a.u.)	2.05 (1.56, 2.22)	1.51 (1.25, 1.98)	2.20 (1.94, 2.73)	0.007 *	0.155	0.023 *
FA (a.u.)	15.04 (9.29, 22.21)	13.42 (9.44, 18.38)	22.32 (11.48, 26.24)	0.298	0.201	0.685
LPE (a.u.)	8.68 (7.16, 11.41)	7.61 (4.77, 12.73)	13.86 (10.32, 17.10)	0.006 *	0.002 *	0.418
LPC (a.u.)	18.48 (13.62, 12.39)	15.75 (8.93, 24.98)	27.37 (22.68, 35.24)	0.006 *	0.001 *	0.396
MG (a.u.)	1.48 (1.02, 2.83)	0.81 (0.48, 1.10)	2.52 (1.77, 3.56)	<0.001 *	0.017 *	0.002 *
PC (a.u.)	46.66 (35.34, 56.80)	41.08 (27.78, 55.27)	53.13 (43.75, 59.73)	0.201	0.257	0.316
PE (a.u.)	7.04 (5.09, 8.78)	4.76 (3.05, 9.53)	6.85 (6.13, 10.46)	0.061	0.573	0.034 *
PI (a.u.)	3.50 (2.86, 4.99)	3.08 (2.09, 5.00)	3.77 (2.70, 6.13)	0.366	0.553	0.307
SM (a.u.)	8.63 (6.13, 10.48)	5.79 (3.13, 10.02)	11.21 (9.65, 12.90)	0.001 *	0.003 *	0.059
TG (a.u.)	24.05 (19.40, 28.94)	21.00 (18.36, 29.71)	22.21 (17.83, 27.27)	0.625	0.381	0.537
Monounsaturated (a.u.)	39.78 (31.30, 47.49)	33.35 (22.55, 46.09)	47.79 (45.98, 60.65)	0.011 *	0.009 *	0.232
Polyunsaturated (a.u.)	93.13 (74.29, 113.90)	78.75 (58.62, 106.44)	104.67 (88.91, 111.74)	0.170	0.233	0.307
Saturated (a.u.)	156.73 (132.57, 189.15)	138.36 (99.15, 168.83)	191.35 (155.78, 203.83)	0.100	0.054	0.452

a.u.: arbitrary units. * $p < 0.05$. HC: healthy control.

Between the three participant groups, there were statistically significant variations in the DG, LPE, LPC, MG, and SM families and monounsaturated lipids (preclinical AD, MCI-AD, and healthy). Additionally, the levels of the Cer, LPE, LPC, MG, and SM families differed statistically significantly between the healthy and preclinical AD groups, while the levels of the DG, MG, and PE differed statistically significantly between the MCI-AD and healthy groups.

Table 3: Analytical method validation.

Analyte	Standard Concentration (nmol L−1)	Recovery (%)	LOD (nmol L−1)	LOQ (nmol L−1)	Linearity Range (nmol L−1)	Equation (y = a + bx) a ± sa b ± sb R2
18:1 LPE	6.25 9.38	8 ± 14 9 ± 15	0.548	1.83	1.83–26.30	0.0019 ± 0.0008 0.0027 ± 0.000063
	12.5	104 ± 17				0.998
18:0 LPC	50 75	153 ± 15 147 ± 15	4.185	13.95	13.95–209.38	0.012 ± 0.024 0.0072 ± 0.00022
	100	134 ± 21				0.997

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16:1 SM (d18:1/16:1)	50 75 100	101 ± 11 101 ± 11 96 ± 16	2.857	9.52	9.52–208.11	0.0774 ± 0.021 0.0064 ± 0.00019 0.997
16:0 SM (d18:1/16:0)	12.5 18.75 25	108 ± 58 102 ± 6 82 ± 5	1.240	4.13	4.13–52.51	−0.0041 ± 0.0063 0.012 ± 0.00024 0.999
18:0 SM (d18:1/d18:0)	3.13 4.69 6.25	100 ± 26 119 ± 59	0.289	0.96	0.96–13.23	0.0014 ± 0.0011 0.0047 ± 0.00017 0.996
18:1 (9-Cis) PE (DOPE)	0.78 1.17 1.56	103 ± 65 62 ± 62	0.069	0.23	0.23–3.30	0.00019 ± 0.00015 0.0024 ± 0.000089 0.996
24:0 SM	6.25 9.38		0.306	1.02	1.02–26.02	0.24 ± 0.03 0.044 ± 0.003
	12.50					0.990

The chosen lipids were 18:1 LPE, 18:0 LPC, 16:1 SM (d18:1/16:1), 16:0 SM (d18:1/d18:0), 18:1 (9-Cis) PE (DOPE), and 24:0 SM based on prior findings. In order to achieve appropriate analytical performance for 18:1 LPE, 18:0 LPC, 16:1 SM (d18:1/16:1), and 16:0 SM (d18:1/16:0), the relevant analytical method was designed and validated. With recoveries around 100%, accuracy was generally good, with the exception of 18:0 LPC, which had recoveries >130%, likely as a result of the matrix effect. A acceptable sensitivity was also attained, with LOQs of 1.83 to 13.95 nmol L1 and LODs between 0.548 to 4.185 nmol L1. The remaining analytes (18:0 SM (d18:1/d18:0), 18:1 (9-Cis) PE (DOPE), and 24:0 SM) did not exhibit adequate analytical performance and were not detected in plasma samples.

Table 4: Lipid concentrations in plasma from participant groups (healthy, MCI-AD, and preclinical AD).

Lipids	Healthy Control (HC) (n = 21)	MCI-AD (n = 35) Median (IQR) (nmol L−1)	Preclinical AD (n = 10) Median (IQR) (nmol L−1)	Kruskal-Wallis p Value (Three Groups)	Mann–Whitney p Value (AD vs. Non-AD)
18:1 LPE	1.37 (0.38, 1.83)	1.8 (1.2, 4.2)	1.8 (0.9, 3.7)	0.010 *	0.003 *
18:0 LPC	67 (61, 80)	65 (56, 96)	81 (60, 105)	0.504	0.569
16:1 SM	15 (7, 27)	13 (8, 24)	19 (15, 25)	0.501	0.647
16:0 SM	177 (137, 206)	168 (132, 213)	209 (159, 239)	0.374	0.371

* p value < 0.05.

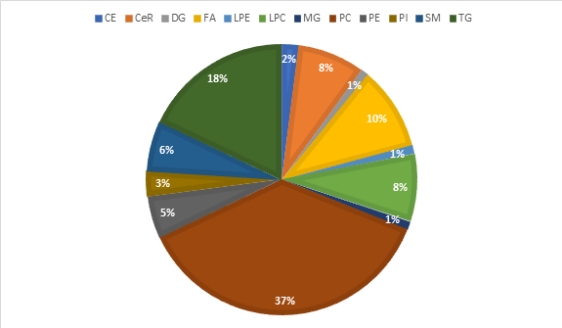

Figure 1: Lipid families discovered through untargeted lipidomic analysis and identification by the LipidMS programme. CE stands for cholesterol esters, Cer for ceramides, DG for diglycerols, FA for fatty acids, LPC for Lys phosphatidylcholines, LPE for Lys phosphatidylethanolamines, MG for monoglycerides, PC for phosphotidylcholines, PE for phosphotidylethanolamines, PI for phosphotidylinositols, SM for Sphingomyelins and TG: Triglycerides.

Plasma samples from healthy individuals (n = 21), patients with preclinical AD (n = 10), and patients with MCI-AD (n = 35) were examined for the presence of a panel of four lipids (already chosen). It provides an overview of the participant groups' lipid concentrations. As can be seen, statistically significant differences for 18:1 LPE were found between the AD (preclinical + MCI) and healthy groups (p = 0.003) as well as across the three groups (p = 0.010). Additionally, t-Tau (0.299, p = 0.022) and p-Tau (0.290, p = 0.026) demonstrated a link with several CSF biomarkers and this possible AD biomarker. It should be noted that there was no association between lipid levels and age.

DISCUSSION

In order to find lipid changes related to the beginning of AD, a lipidomic method was created in plasma samples from participants categorised according to their amyloid status (CSF biomarkers). In this, comparisons between early AD (preclinical or MCI) and healthy participants were assessed using an untargeted technique. Lipid families were examined, and some relevant factors in early AD dysregulation were found.[8]

Finally, to find other potential discriminating variables, a supplemental multivariate analysis was conducted. The Lipid MS database's identification of lipid families showed that DG, LPE, LPC, MG, and SM may have played a role in early AD. Some lipid

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families (Cer, LPEs, LPCs, MGs, and SMs) were identified as prospective biomarkers in the comparison of preclinical AD and healthy groups because they were differentially expressed, particularly the monounsaturated species. Similar findings were made by Mielke et al. between Cer and SMs and the risk of AD, albeit they did note distinct hazards for men and women. Ceramides' function as mediators of neuronal death linked to oxidative stress. A buildup was also discussed by Jazvin'cakJembrek et al. As a result, this dysregulation of ceramides in the disease's preclinical phases may hasten the development of clinical symptoms that cause neuronal death.[8,9] Additionally, Panchal et al. described the buildup of ceramide in AD plaques. Ceramide and SM have also been linked to cognitive loss in AD. Ceramides' usefulness as dementia biomarkers, however, needs more research. Although our findings indicate that LPE may be a possible diagnostic for preclinical stages, it was previously reported as a biomarker for progression to AD. Similar to this, LPCs might be a biomarker for AD in its early stages. In this way, LPCs are involved in the transport of polyunsaturated fatty acids (PUFAs) across the blood–brain barrier, possibly regulating the availability of these vital substances for brain health. Different lipid families (DGs, MGs, and PEs) were found to be promising biomarkers in the comparison of MCI-AD and healthy controls.[9,10]

Similar to this, Wood et al. discovered elevated DG and MG levels in early AD. Due to their participation in cellular processes such oxidative phosphorylation, mitochondrial biogenesis, and autophagy, PEs may play a role in the physiopathology of AD. MGs may serve as possible biomarkers of early AD, including the preclinical and MCI-AD stages, according to our findings. The preclinical stage also appears to specifically modify LPE, LPC, and SM, while DGs may serve as biomarkers for the MCI stage.[11] The annotation of variables using several databases, such as HMDB, Kegg, and Metlin, however, revealed additional significant annotated variables and metabolite classes. Some lipid families, including phosphatidylglicerol, glicerophosphocholine, glicerophosphoserine, phosphoethanolamine, phosphocholine, glicoesphingolipid, diacilglicerol, terpenes, steroids, flavonoid classes, and vitamin E, were found to distinguish preclinical AD from healthy subjects. Specifically, plasma glycerophosphocholine compounds were seen at higher levels in the preclinical AD Similar to this, other investigations found higher levels of this lipid in the brains of AD patients as well as in samples of their cerebrospinal fluid, showing that AD is characterised by aberrant phospholipid metabolism in the brain.[11,12] Additionally, the preclinical AD group had lower plasma phosphoethanolamine levels according to the current study, and lower PE levels were discovered in AD brain tissues in a prior investigation. In actuality, PE serves as both a substrate for crucial posttranslational changes and a precursor for phosphatidylcholine. Furthermore, the preclinical AD group had greater amounts of phosphocholine, a precursor to phosphatidylcholine, suggesting a potential membrane disruption in the early disease process.[12,13]

Furthermore, increased quantities of glycosphingolipids were found in the plasma samples from these patients, suggesting that they may have a role in preclinical AD. Ceramides, which are involved in the metabolism of sphingolipids, demonstrated a relationship with neuropsychiatric symptoms in this regard.[14] Furthermore, we discovered greater DG levels in the preclinical AD group, which are comparable to the elevated plasma levels in early AD, indicating that lipidomics changes cause DG accumulation in MCI participants. Phosphatidylglycerol (PG) and flavonoids, on the other hand, exhibited reduced plasma levels in the preclinical AD group in the current investigation. The inhibition of microglia activation and A aggregation by flavonoid drugs may have an anti-AD pathological effect. As a result, a decrease in these substances at the beginning of the disease may aid in the creation of AD pathways. According to studies, preclinical AD patients had higher amounts of vitamin D than healthy individuals, but our research revealed that earlier studies had identified lower levels of these vitamins in AD and MICAD cases.[14,15]

The preclinical AD status of the individuals reviewed here raises the possibility that this group was displaying a compensatory reaction to the disease process. The putatively annotated biomarkers 1-O-palmitoyl-2-O-acetyl-sn-glycero-3-phosphorylcholine and pisumionoside also contribute to the distinction between preclinical AD and healthy controls.[16] An exogenous substance called pisumionoside, which is generated from plants like garden pea seedpods, may have hepatoprotective properties. When compared to people with preclinical AD, these levels are higher in healthy subjects. Pisumionoside might therefore be protective against AD. Additionally, in keeping with earlier investigations, the glycerophosphorylcholine (1-O-palmitoyl-2-O-acetyl-sn- glycero-3-phosphorylcholine revealed elevated levels in AD. In other illnesses like multiple sclerosis, its oxidised products were regarded as indicators of neuroinflammation.[16,17] In addition, HMDB annotated other lipid families (such as glycosyldiacylglycerols, fatty acids, terpenoids, sesquiterpene mycotoxins, terpene lactones, phosphocholines, glucosylceramides, and fucopentanoses) when comparing MCI-AD and healthy groups.

First, the MCI-AD group had decreased levels of glycosyldiacylglycerols. In previous research, it was discovered that neurodegenerative illnesses including AD and dementia with Lewy bodies cause an increase in the diacylglycerols in the frontal cortex. Additionally, a connection between AD and glycosylation and neurodegeneration was found. As a result, it can be a sign of illness development.

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Additionally, the MCI-AD group had lower amounts of fatty acids than in earlier publications, which reflected dietary and metabolic changes. Terpenoids and a few vitamins also appeared in increased concentrations in the MCI-AD group. Since earlier research found that these chemicals had protective benefits, there is considerable debate in this regard.[17]

Regarding the focused analysis, the new analytical approach was able to identify low plasma levels of certain lipids (18:1 LPE, 18:0 LPC, 16:1 SM (d18:1/16:1), and 16:0 SM (d18:1/16:0) that may be relevant as potential AD biomarkers. For each of them, accuracy was acceptable. In contrast to healthy controls, only 18:1 LPE demonstrated statistically significant elevated levels in preclinical and MCI-AD. Su et al. discovered that extracellular vesicles produced from the brain of AD patients had more of this lipid. An earlier investigation of LPC in plasma samples revealed a rise with ageing, which is particularly pronounced in AD circumstances. Similarly, the current investigation discovered decreased levels of L-phosphatidilcholine and PC and increased amounts of LPC 18:1 in AD patients. Mulder et al. did discover a decline in the LysoPC/PC ratio in MCI or dementia brought on by AD circumstances.[17] The current study additionally revealed plasma 18:1 LPC correlations with CSF Tau and p-Tau, which are biomarkers commonly used in AD diagnosis. Tau is specifically regarded as a biomarker for neurodegeneration. In this way, the relationship between 18:1 LPC and Tau indicated the potential value of 18:1 LPC as a biomarker for neurodegeneration. Similar to this, earlier research demonstrated the potential value of the metabolites 18:0 LPC and 18:2 LPC as biomarkers for AD.[17,18] These inconsistencies might be explained by the various sample types employed (plasma and CSF), as well as by the various isomers identified in the families of these chemicals. Additionally, the plasma samples' LPC to PC ratio demonstrated the ability to distinguish between persons with AD and those without AD.[18,19] The tiny sample size of this study is its principal drawback. However, using neuroimaging, the participants were precisely divided into groups based on their amyloid status, cognitive state, and brain abnormalities. Furthermore, there aren't enough follow-up investigations to recognise the metabolites as trustworthy AD biomarkers. However, this work offers a thorough lipidomic strategy from untargeted and targeted analysis that revealed potential biomarkers and pathways involved in the onset of AD. Age and lipids or lipid classes were correlated, even though assessments of confounding factors like age were not done.[19,20]

CONCLUSION

From both untargeted and targeted studies of plasma samples, a lipidomic technique was created. It revealed some differences in the expression of lipids between individuals with early-stage AD and healthy volunteers. In order to detect AD early and with little to no invasiveness, the plasma lipid profile may be helpful. Among the lipid families, DGs, LPEs, LPCs, MGs, and SMs produced pertinent data. Particularly, MGs may be helpful in the early detection of AD, whereas LPEs, LPCs, and SM are more closely related to their preclinical stage and DGs are more closely related to the MCI stage. Among these families, 18:1 LPE demonstrated potential use as an AD and neurodegeneration biomarker. Other analyte families, including phosphatidylglycerol, phosphocholine, glicerophosphocholine, glicerophosphoserine, glicoesphingolipid, vitamin E, terpenes, steroids, flavonoids, glycosyldiacylglycerols, fatty acids, glucosylceramides, and fucopentanoses, also demonstrated potential alterations in the early stages of AD. However, these early findings need to be confirmed by additional investigation on a large number of samples.

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