Correlation of Short Chain Fatty Acid Levels in Patients Non-Alcoholic Fatty Liver Disease with Obesity

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ABSTRACT

***Background**: NAFLD has the potential to develop into severe diseases like NASH and cirrhosis and is often linked to obesity, although it can also occur in non-obese individuals, complicating diagnosis. SCFAs, produced by intestinal bacteria through the fermentation of dietary fibers, are essential for metabolic health and may influence liver fat and weight regulation. The purpose of this study was to explore the connection between SCFA levels and the severity of NAFLD, including liver fibrosis, in individuals both with and without obesity.*

***Methods**: A cross-sectional investigation of 16 NAFLD patients with obesity and 11 without, with stool samples analyzed for SCFA via gas chromatography. Obesity was defined by abdominal circumference. Data were analyzed using Spearman's correlation, Eta's correlation, and Pearson's test.*

***Results**: Levels of SCFAs, including butyrate, propionate, and acetate, were significantly correlated in both obese and non-obese individuals diagnosed with NAFLD (r=0.618, p=0.001; p=0.019; p=0.037; p=0.012). Obesity was found to be positively associated with the severity of NAFLD (r=0.582, p=0.001). However, obesity did not exhibit a statistically significant connection with liver fibrosis (p = 0.351).*

***Conclusion**: Obese NAFLD patients exhibited decreased SCFA levels compared to non-obese individuals. Central obesity was linked to NAFLD severity but not fibrosis progression. SCFAs and obesity are crucial in the pathogenesis of NAFLD.*

***Keywords**: Central Obesity, Gut Microbiota, NAFLD, SCFA*

ABSTRAK

***Latar belakang**: NAFLD memiliki potensi untuk berkembang menjadi penyakit yang lebih parah seperti NASH dan sirosis. NAFLD sering dikaitkan dengan obesitas, meskipun dapat juga terjadi pada individu non-obesitas, yang membuat diagnosis NAFLD pada pasien non-obesitas menjadi lebih sulit. SCFA yang diproduksi oleh bakteri usus dari fermentasi makanan berserat, sangat penting untuk*

metabolisme lemak di hati dan regulasi berat badan. Penelitian ini bertujuan untuk menilai hubungan antara kadar SCFA dan tingkat keparahan NAFLD, termasuk fibrosis hati, pada individu dengan dan tanpa obesitas.

***Metode**: Penelitian potong lintang dilakukan pada 16 pasien NAFLD dengan obesitas dan 11 pasien tanpa obesitas, dengan sampel tinja dianalisis untuk SCFA menggunakan kromatografi gas. Obesitas didefinisikan berdasarkan lingkar perut. Data dianalisis menggunakan korelasi Spearman, korelasi Eta, dan uji Pearson.*

***Hasil**: Kadar SCFA, seperti butirat, propionat, dan asetat, mempunyai korelasi yang bermakna dengan pasien obesitas dan non-obesitas dengan NAFLD (r=0.618, p=0.001; p=0.019; p=0.037; p=0.012). Obesitas mempunyai asosiasi positif dengan tingkat keparahan NAFLD (r=0.582, p=0.001). Namun, tidak didapatkan hubungan yang bermakna antara obesitas dan fibrosis hati (p = 0.351).*

***Simpulan**: Pasien NAFLD yang obesitas menunjukkan penurunan kadar SCFA yang lebih rendah dibandingkan dengan individu non-obesitas. Obesitas sentral berhubungan dengan tingkat keparahan NAFLD tetapi tidak dengan progresi fibrosis. SCFA dan obesitas memainkan peran penting dalam patogenesis NAFLD.*

***Kata kunci**: Mikrobiota Usus, NAFLD, Obesitas Sentral, SCFA*

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) comprises a spectrum of liver disease, from fat accumulation in the liver (hepatic steatosis) to a more severe form called non-alcoholic steatohepatitis (NASH), which may cause progressive fibrosis and progress to cirrhosis.[1] In some cases, NAFLD can ultimately lead to the onset of cirrhosis or hepatocellular carcinoma as it progresses. Key metabolic factors like obesity, insulin resistance, and high blood pressure play a major role in driving disease-related complications in affected individuals.[2]. The rise in obesity, driven by lifestyle changes, Westernized diets, and urbanization, particularly in Asia, parallels the increasing global burden of NAFLD.[3] Today, NAFLD stands as among the liver conditions most commonly identified across the globe and remarkably high frequency observed in the broader population, underscoring its significant public health impact.

Most individuals with NAFLD present with simple steatosis, which typically does not impact the development of liver related events. However, approximately 5-10% may progress to Non-Alcoholic Steatohepatitis (NASH), with 38% at risk of fibrosis and 30% potentially progressing to cirrhosis [4]. Some data also suggest that NAFLD may impact cardiovascular mortality[3]. Although commonly associated with obesity, NAFLD is also found in non-obese individuals, highlighting its complexity in pathogenesis and clinical management. Non-obese NAFLD patients often present with central obesity and remain vulnerable to disease progression.[5] Factors such as gut microbiota dysbiosis and insulin resistance play a crucial role in the development of NAFLD in non-obese individuals[6,7].

Gut microbiota, particularly short-chain fatty acids (SCFAs), are increasingly recognized for their role in NAFLD progression. SCFAs are produced when gut bacteria ferment dietary fibers and contribute to intestinal homeostasis, metabolism regulation, and immune function. Studies have shown that SCFAs play a role in lipogenesis, gluconeogenesis, and satiety, influencing hormones like PYY, GLP-1, and ghrelin, which regulate appetite and weight loss. However, the role of SCFAs in liver diseases remains underexplored. [8] This study aims to investigate the SCFA profiles in NAFLD patients with and without obesity to better understand their role in the disease's progression and their link to obesity.

METHODS

Study Design

This study utilizes an observational analysis with a cross-sectional research design. The participants in this study were drawn from a group of patients with confirmed NAFLD diagnoses at the Gastroenterology and Hepatology Clinic of RSUD dr. Saiful Anwar Malang. The study was conducted over a period of approximately 6 months, from October 2022 to March 2023, until the required sample size was achieved

Ethical Clearance

This study adhered to established ethical research standards and obtained formal authorization from the RSSA Health Research Ethics Committee under reference number 400/065/K.3/102.7/2022. Prior to the commencement of the study, all participants were comprehensively briefed about the research, including its objectives, procedures, and any potential risks, to ensure their understanding. After understanding the information, participants signed the informed consent form.

Participants and Eligibility Criteria

Consecutive sampling was employed to ensure that the exclusion and inclusion criteria were fulfilled until the necessary sample size was reached. The target population in this study consisted of adult patients (18–50 years) with confirmed NAFLD based on abdominal ultrasound results, both with and without central obesity. The patients were subsequently divided into three categories according to the severity of their fatty liver: mild, moderate, and severe.[10] The exclusion criteria for this research involved individuals with a background of alcohol use or use of medications known to cause fatty liver (corticosteroids, amiodarone, tamoxifen, methotrexate, and antidepressants). Patients with a history of probiotic intake or medications that can cause gut microbiota dysbiosis (antibiotics, PPIs, NSAIDs, opioids, and antipsychotics) within two weeks preceding the study were also omitted. Additional exclusion criteria included patients with viral hepatitis B or C infections, hepatocellular carcinoma, congenital liver abnormalities, or other autoimmune liver diseases.

Data Collection

The Lemeshow formula was employed to calculate the appropriate sample size for this study

$$= \left[\frac{(Z\alpha+Z\beta)}{0{,}5ln\left(\frac{1+\tau}{1-\tau}\right)}\right]^2 + 3$$

(n = the number of subjects, Alpha (α) = Type I error was set at 5% with a one-tailed hypothesis, Z α = The standard value from the distribution corresponds to the α value = 1,64 %, Beta (β)= Type II error was set at 10%, Z β = The standard value of beta = 1,28, r= The minimum correlation coefficient considered significant was set at 0.55. In this investigation, the sample size was determined to need at least 26 NAFLD patients. During the study, 5 participants were excluded due to non-compliance with inclusion criteria and voluntary withdrawal, which had been anticipated in the study design, resulting in a final sample size of 27, still meeting the required minimum size of NAFLD patients.

Measure

In this study, central obesity is characterized by a waist-to-height ratio (WHR) size greater than 88 cm for women and 102 cm for men.[9] SCFA levels, including acetate, propionate, and butyrate, were assessed in patient faecal samples using gas chromatography analysers at Prodia Laboratory, Malang. SCFA levels were expressed in mmol/L. Liver fibrosis was assessed using Transient Elastography (TE) using the XL probe for obese patients, with the Fibro Scan Expert 630 and VCTE™ technology, and performed by a gastroenterology-hepatology consultant.

Statistical Analysis

The analysis of all measurement results in this study was performed using the computer software IBM SPSS Statistics 28. The procedure for testing comparative and correlational hypotheses was outlined as follows: data normality testing, multivariable comparative analysis using methods such as Chi-square, Mann-Whitney, Independent t-test, and Likelihood Chi-square, as well as correlation testing using methods such as Spearman correlation, Eta correlation, and Pearson correlation. With a significance criterion of 0.05 ($p < 0.05$) and a 95% confidence margin ($\alpha = 0.05$).

RESULTS

Patients Selection

A total of 27 NAFLD patients participated in this study, with 16 assigned to the Obesity group and 11 to the Non-Obesity group. For the Obesity group, the average age was 39±13.74 years, whereas the Non-Obesity group had an average age of 43±15.23 years. The majority of participants in both groups were male, making up 56.3% of the Obesity group and 63.6% of the Non-Obesity group.

Baseline Characteristics

Comorbidities were more prevalent in the Obesity group, with 55.6% having hypertension compared to 44.4% in the Non-Obesity group. Dyslipidaemia was also more common in the Obesity group (66.7% vs 33.3%). However, the occurrence of metabolic syndrome and diabetes mellitus was consistent across both groups, with 50% of participants in each group affected.

Anthropometric measurements showed that the Obesity group had a higher mean upper arm circumference (33.81±3.83 cm) compared to the Non-Obesity group (27.64±4.85 cm). The Obesity group exhibited a greater body fat percentage (32.41±5.86%) than the Non-Obesity group (28.00±6.83%). Conversely, muscle mass percentage was somewhat reduced in the Obesity group (26.10±4.59%) when compared to the Non-Obesity group (28.15±4.34%). Additionally, blood pressure readings were elevated in the Obesity group in comparison to the Non-Obesity group.

Table 1. Basic Characteristics of Study Samples Based on Obesity Status in NAFLD

Variable	Obesity (N = 16)	Non-Obesity (N = 11)	*p*
Age, yr – mean (SD)	39 ±13.74	43±15.23	0.674[d]
Gender – n (%)			
Female	7 (63.6)	4 (36.4)	0.701[a]
Male	9 (56.3)	7 (43.8)	
Comorbidities– n (%)			
Hypertension	5 (55.6)	4 (44.4)	0.601[a]
Dyslipidemia	14 (66.7)	7 (33.3)	0.782[a]
Diabetes Mellitus	3 (50)	3 (50)	0.143[a]
Metabolic Syndromes	8 (50)	8 (50)	0.238 [a]
Body Roundness Index (BRI)– mean (SD)			
Height, cm	163.06±8.46	165.45±8.13	0.470[c]
Weight, kg	89.97±12.28	64.52±11.05	0.000[c]
Waist Size, cm	108.53±7.83	91.23±4.87	0.000[c]
Upper Arm Size, cm	33.81±3.83	27.64±4.85	0.001[c]
Body Fat Mass, %	32.41±5.86	28.00±6.83	0.085[c]
Body Muscle Mass, %	26.10±4.59	28.15±4.34	0.190[d]
Body Mass Index, kg/m^2	33.81±4.34	23.77±3.37	0.000[d]
Blood Pressure – mean (SD)			
Systolic, mmHg	134.81±17.82	131.91±13.29	0.786[d]
Diastolic, mmHg	82.00±12.72	81.91±6.06	0.983[c]
Laboratory Findings – mean (SD)			
Hemoglobin, mg/dl	14.66±1.41	14.75±1.60	0.876[c]
Leukocytes, x10^3 cells/mm^3	7.53±1.61	6.47±1.54	0.099[c]
Platelets x10^3 cells/mm^3	340.75±5.70	316.45±7.54	0.349[c]
Fasting Blood Glucose, mg/dl	111.06±43.94	111.00±28.13	0.997[c]
Total Cholesterol, mg/dL	217.56±44.32	201.73±56.12	0.311[d]
LDL, mg/dL	147.38±37.08	136.45±44.92	0.496[c]
HDL, mg/dL	46.13±12.40	51.00±12.77	0.331[c]
Triglycerides, mg/dL	188.38±52.25	145.00±65.25	0.067[c]
HbA1c, (%)	6.14±1.84	6.63±1.94	0.334 [d]
SGOT, U/L	31.48±17.96	30.42±13.25	0.869[c]
SGPT, U/L	38.67±22.47	38.39±23.33	0.975[c]
Direct Bilirubin, U/L	0.22±0.07	0.17±0.04	0.060 [d]
Total Bilirubin, U/L	0.55±0.24	0.45±0.13	0.193[c]
Alkaline Phosphatase, U/L	67.49±35.70	84.27±15.08	0.374 [d]
Gamma-glutamyl Transferase, U/L	54.48±33.89	57.05±15.88	0.657 [d]
Albumin, g/dl	4.56±0.42	4.69±0.34	0.411[c]
Degree of NAFLD, n (%)			
Mild Fatty Liver	7 (43.8)	11 (100)	0.010[b]
Moderate Fatty Liver	1 (6.3)	0	
Severe Fatty Liver	8 (50.0)	0	
Liver Fibrosis, kPa – mean (SD)	6.87±2.47	5.39±1.20	0.079 [c]

*NAFLD, *Non-alcoholic fatty liver disease*; HDL, *High density lipoprotein;* HbA1c, *Haemoglobin* A1c; LDL, *Low density lipoproteins*; SGOT, *Serum Glutamic Oxaloacetic Transaminase*; SGPT, *Serum Glutamic Pyruvic Transaminase*. Data were analysed using [a]Chi-square test, [b]*Likelihood Ratio Chi-Square*, [c]*Independent T-test*, [d]Mann Whitney test (d).

Obese patients showed higher levels of fasting blood glucose, total cholesterol, LDL, and triglycerides, as revealed by laboratory tests. Meanwhile, significant variations in HbA1c, albumin, and liver enzymes were observed between the two groups. The Obesity group exhibited a greater prevalence of NAFLD (59.3% vs. 40.7%). Ultrasonography showed that the Non-Obesity group mostly had mild fatty liver, while moderate and severe fatty liver were seen only in the Obesity group. Liver fibrosis evaluation through transient elastography showed that the average liver stiffness was notably greater in the Obesity group (6.87±2.47 kPa) than in the Non-Obesity group (5.39±1.20 kPa)

Main Findings

Table 2 shows a significant positive relationship between NAFLD severity and obesity, with a Spearman correlation coefficient of 0.582 and a p-value of 0.001, indicating a strong association at a 99% confidence level ($p< 0.01$). This correlation implies that individuals with greater obesity levels are more likely to have severe NAFLD, suggesting that obesity contributes to the progression of NAFLD to more advanced stages.

Table 3 shows a correlation between obesity and liver fibrosis values in NAFLD patients. The average liver stiffness in the Obesity group was 6.87 ± 2.47 kPa, while in the Non-Obesity group, it was 5.39 ± 1.20 kPa. Even though the Obesity group had a greater average liver fibrosis value, statistical testing indicated that the correlation was not statistically significant ($p = 0.351$). The η^2 value of 0.898 suggests some variation in liver fibrosis related to obesity status, but the strength of this relationship was not strong enough to reach statistical significance at the established confidence level ($p < 0.05$).

The data in **Table 4** show that total SCFA levels were higher in the non-obese NAFLD group (9.43±2.08 mg/dL) than in the obese group (7.52±1.75 mg/dL), with a significant difference (p=0.001) and a strong positive correlation (r=0.618). Additionally, levels of acetic acid, butyrate, and propionate were also elevated in the non-obese group, each showing a p-value of less than 0.05 and a positive correlation. These findings indicate that non-obese NAFLD patients exhibit higher SCFA levels, which may contribute to the characteristics observed in this group.

Table 2. The Relationship Between Obesity and the Degree of NAFLD

Degree of NAFLD	Obesity (N = 16)	Non-Obesity (N = 11)	*r*	*p*
Mild Fatty Liver	7 (43.8)	11 (100)		
Moderate Fatty Liver	1 (6.3)	0	5.82	0.001[a]
Severe Fatty Liver	8 (50.0)	0		

[a]*Spearman's rank correlation test; *p<0.05 significancy*

Table 3. The Relationship Between Obesity and Liver Fibrosis in NAFLD Patients

Variable	Obesity (N = 16)	Non-Obesity (N = 11)	η^2	*p*
Liver Fibrosis, kPa – mean (SD)	6.87±2.47	5.39±1.20	0,898	0.351 [a]

[a]*Eta correlation test; *p<0.05 significancy*

Table 4. The Relationship of SCFA Levels in NAFLD Patients with Obesity and Non-Obesity

Variable	NAFLD Group		*p*	*r*
	Obesity (N=16)	Non-Obesity (N=11)		
Levels SCFA, mean±SD				
Total SCFA Levels, mg/dL	7.52±1.75	9.43±2.08	0.001*	0.618[a]
Acetic Acid, mg/dL	4.61±1.19	5.57±1.63	0.012*	0.478[a]
Butyrate Acid, mg/dL	1.36±0.68	1.65±0.42	0.019*	0.450[a]
Propionate Acid, mg/dL	1.55±0.56	2.01±0.49	0.037*	0.403 [a]

[a]*Pearson correlation; *p<0.05 significancy*

DISCUSSION

This study found significant differences in various anthropometric measures related to obesity, including waist circumference, body weight, upper arm circumference, and Body Mass Index (BMI), between NAFLD patients with obesity and those without obesity. This observation supports the definition of central obesity, where waist circumference is a key indicator. The greater waist circumference in the obesity group signifies an accumulation of abdominal fat, which is commonly linked to an increased risk of metabolic conditions, including NAFLD.[11]

In addition, the higher body weight and BMI in the obesity group reflect an excess of total body mass, which is a critical risk factor in the onset of NAFLD. These notable differences emphasize the important role of anthropometric measurements in distinguishing the risk profiles of NAFLD patients between the obesity and non-obesity groups. This supports the notion that central obesity plays an essential role in the advancement of NAFLD.[11]

Based on the anthropometric data, the waist circumference was notably higher in obese patients compared to those without obesity, with an average of 108.53 ± 7.83 cm in the obese group and 91.23±4.87 cm in the non-obese group. An enlarged waist circumference serves as a primary marker of central obesity, a significant risk factor for NAFLD.[12] Likewise, the BMI was considerably greater in the obesity group., averaging 33.81 ± 4.34 kg/m², compared to 23.77 ± 3.37 kg/m² in the non-obesity group. This suggests a strong link between elevated BMI and a heightened risk of developing NAFLD.[13]

Upper Arm Circumference (UAC) in obese patients was also found to be significantly higher compared to non-obese patients. UAC is an important marker strongly associated with MetS (Metabolic syndrome), which includes central obesity, insulin resistance, hypertension, and dyslipidemia—conditions that often accompany NAFLD in obese patients. The buildup of subcutaneous fat in the upper arm could potentially trigger insulin resistance and inflammation, which in turn contribute to metabolic dysfunction.[14] Higher UAC has been has been associated with higher liver fat content and greater liver stiffness, indicators of fibrosis that worsen NAFLD severity.[15]

The study revealed that obese patients generally exhibited greater fatty liver severity compared to non-obese individuals. These findings are consistent with Lonardo's research, which highlights obesity plays a pivotal role in the advancement of NAFLD to its more severe forms, including moderate and severe fatty liver. Obesity is closely associated with increased visceral fat in the liver, a significant contributor to the development of more severe liver conditions.

Central obesity, indicated by waist circumference, is a more important risk factor for NAFLD than BMI, as visceral fat is more metabolically active and functions as a fundamental factor in inflammation and insulin resistance, contributing to the progression of more severe liver conditions.[16] Studies indicate that visceral fat is more relevant in describing NAFLD risk in younger Southeast Asian populations.[17,18]

This study found that obesity, particularly central obesity, is associated with more severe steatosis in NAFLD. These results align with previous research that supports the connection between central obesity and the progression of NAFLD. For example, a study by Jingjing showed that abdominal obesity greatly increases the likelihood of developing NAFLD. Those with central obesity were more prone to developing NAFLD than individuals without this condition. The study indicated that central obesity promotes insulin resistance and systemic inflammation, which in turn drive the progression of NAFLD.[18]

A study by Najafi highlighted that individuals with central obesity, irrespective of their metabolic health condition, had an elevated risk of NAFLD. This suggests that central obesity acts as an autonomous risk factor in the progression of NAFLD, particularly in those with metabolic syndrome. These findings highlight the crucial role of fat distribution, especially visceral fat associated with central obesity, in the progression of NAFLD.[19]

Obese patients were found to have lower SCFA levels compared to non-obese patients, suggesting alterations in gut microbiota that influence lipid and glucose metabolism [13]. The lower levels of acetic acid and propionate in obese patients were associated with insulin resistance and impaired energy regulation.[6,7] Additionally, decreased butyrate levels contribute to increased gut permeability and systemic inflammation.[6] As seen in **Figure 1**, these mechanisms are visually represented, demonstrating how dysbiosis and SCFA imbalances contribute to the progression of NAFLD.

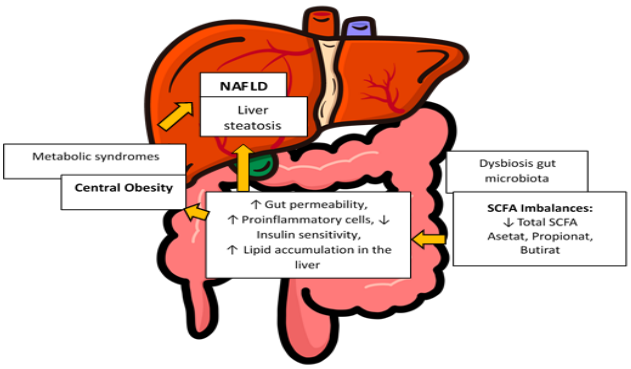

Figure 1. Pathomechanism SCFA in NAFLD with Central Obesity

Liver fibrosis in NAFLD is often associated with obesity, particularly central obesity, which elevates free fatty acid levels and insulin resistance, exacerbating liver inflammation [12]. However, in this study, although obesity was linked to the distribution of advanced fibrosis stages (F2 and F4), the correlation was not statistically significant (r=-0.345, p=0.078). This differs from findings by Jingjing[18], which indicated that central obesity accelerates fibrosis progression through metabolic and inflammatory mechanisms.

The study also found differences in SCFA levels between obese and non-obese NAFLD patients. Non-obese patients generally had higher levels of SCFAs, including acetic acid, butyrate, and propionate. The presence of elevated SCFA levels in non-obese patients may be associated with insulin resistance and gut microbiota alterations, both of which are factors that could contribute to the development of NAFLD, even in individuals with a normal body weight. [20,21] Furthermore, Kolodziejczyk noted that genetic factors, abnormal fat distribution, or changes in gut microbiota also play important roles in non-obese NAFLD.[13]

Conversely, obese patients exhibited lower SCFA levels, reflecting more severe gut microbiota dysbiosis, which contributes to NAFLD progression through increased fat accumulation in the liver.[22] Reduced SCFA production in obesity may be due to dietary changes and other metabolic factors that impact gut microbiota. [23,24] These contrasting patterns highlight distinct mechanisms underlying NAFLD development in obese and non-obese patients. Additional studies are required to clarify these causal relationships , focusing on the role of gut microbiota and SCFA metabolism in non-obese individuals. Investigating potential SCFA-based therapeutic approaches could provide valuable insights into managing NAFLD, particularly in non-obese patients.

Acetate, propionate, and butyrate play critical roles in regulating metabolism and preventing NAFLD. Acetate helps regulate appetite, enhance fat oxidation, improve glucose homeostasis, and reduce inflammation. As a lipogenic substrate, acetate supports lipogenesis in the liver, which can increase adipogenesis in obese individuals while reducing food intake [8,25]. Propionate functions to suppress appetite and food intake, enhance pancreatic function, inhibit hepatic de novo lipogenesis, and increase the release of GLP-1 and PYY hormones critical for appetite regulation. [25,26]

Butyrate reduces food intake and improves glucose profiles through interactions with brain-gut neural circuits. It also boosts energy expenditure by enhancing mitochondrial activity in skeletal muscle and facilitating the breakdown of fat in adipose tissue.[25] Recent research indicates that the ratio of SCFAs in the body may influence metabolic health, with a higher ratio of acetate to butyrate and propionate contributing to an increased risk of NAFLD. This relationship highlights the importance of the gut microbiome and its role in SCFA metabolism in NAFLD progression. Further studies are necessary to explore how the balance of SCFAs, particularly in non-obese individuals, contributes to the development and progression of NAFLD. Investigating the pathways involved in SCFA metabolism through microbiome analysis and metagenomics could provide valuable insights into potential therapeutic approaches[27]

Among the limitations of this study are the small sample size, which may reduce the robustness of the results and their extrapolation to the general population. Additionally, the use of a cross-sectional design limits the capacity to establish cause-and-effect relationships between obesity, SCFA levels, and NAFLD progression, highlighting the need for further research.

CONCLUSION

Longitudinal studies with larger sample sizes are needed to enhance statistical power and generalizability. Future research should control for confounders like diet, physical activity, and medication use to better isolate the effects of obesity and SCFAs on NAFLD. Additionally, direct measurement of gut microbiota composition would provide deeper insights into dysbiosis and its role in NAFLD progression. A more detailed exploration of how SCFAs influence NAFLD could further contribute to understanding their impact on liver function.

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