

A Comprehensive Review of Metformin Use in Non-Alcoholic Fatty Liver Disease (NAFLD) with Insights from a Student-Based Survey

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Abstract

This study combined a literature review and survey results from 41 first-year pharmacy students to assess their understanding and opinions on the use of metformin in the management of non-alcoholic fatty liver disease (NAFLD), achieving a high response rate of 92%. NAFLD affects approximately 25% of the global population and is commonly associated with conditions such as obesity, dyslipidemia, and type 2 diabetes, making it a major public health concern. Metformin, primarily used for type 2 diabetes, has received attention for its potential to improve insulin sensitivity and reduce hepatic glucose production, suggesting a possible role in NAFLD treatment. Survey data were analyzed using SPSS software, revealing demographic differences in knowledge and attitudes. Participants aged 18–24 years showed greater familiarity with metformin than older respondents. Female students were more likely to support metformin use in NAFLD and had a better grasp of its benefits compared to males. In addition, those who were employed and lived outside specific states showed higher awareness, indicating possible regional disparities in knowledge. Students with a 4-year degree showed greater familiarity with the role of metformin in the treatment of NAFLD. These findings emphasize the need for targeted educational strategies to address knowledge gaps and suggest incorporating NAFLD management into pharmacy curricula. Statistically significant associations were found between students' demographic factors—such as age, gender, employment status, residency, and income—and their understanding of metformin, suggesting diverse educational needs across subgroups.

Keywords: Non-Alcoholic fatty liver disease, Metformin, Pharmacy education, Student survey

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a widespread condition marked by the excessive accumulation of fat in the liver, encompassing a spectrum from simple fatty liver (steatosis) to its more severe forms, such as non-alcoholic steatohepatitis (NASH) and liver cirrhosis. Affecting nearly a quarter of the global population, NAFLD is emerging as a critical public health issue, strongly associated with metabolic risk factors like obesity, dyslipidemia, insulin resistance, and type 2 diabetes.

Although there is currently no definitive cure for NAFLD, a variety of treatment strategies have proven effective in managing and potentially reversing the disease. The primary approach involves lifestyle interventions—adopting a balanced diet rich in whole grains, fruits, and vegetables while limiting saturated fats and sugars, engaging in regular physical activity, achieving moderate weight loss, and eliminating harmful habits such as smoking. Depending on the stage and individual profile of the patient, pharmacologic treatments may also be recommended. For example, vitamin E has shown promise in treating NASH, and medications such as pioglitazone, GLP-1 receptor agonists, and statins may be employed under certain conditions. In advanced cases where liver damage is severe, liver transplantation might become necessary. Effective management also requires addressing coexisting conditions like diabetes and obesity, along

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with regular monitoring to prevent disease progression and complications.

Metformin, widely prescribed for managing type 2 diabetes due to its insulin-sensitizing properties, has recently garnered attention as a potential treatment for NAFLD. This review aims to synthesize current literature on metformin's effectiveness in NAFLD management, analyzing findings from both clinical studies and experimental research. Special emphasis is placed on its underlying mechanisms of action, particularly the activation of AMP-activated protein kinase (AMPK), which plays a central role in reducing hepatic glucose production, improving insulin sensitivity, and suppressing the synthesis of cholesterol and fatty acids. Duseja *et al.* [1] conducted a forward-looking clinical investigation to evaluate the therapeutic potential of metformin in individuals with non-alcoholic fatty liver disease (NAFLD) who had not responded to lifestyle modifications alone. Although the study does not specify the exact sample size, it focused on a population resistant to traditional interventions such as dietary changes and exercise. The findings indicated that metformin may help enhance liver function and reduce hepatic fat in these difficult-to-treat cases.

In another study, Targher and Byrne [2] examined the complex interplay between NAFLD and chronic kidney disease (CKD), emphasizing how each condition may influence the development and progression of the other. Their review of existing research underlined the importance of developing integrated, multidisciplinary care strategies for patients suffering from both conditions.

Li *et al.* [3] conducted a comprehensive systematic review and meta-analysis that examined metformin's impact on NAFLD. Their findings suggested that metformin could be effective in improving not only liver-related outcomes but also broader metabolic parameters. Complementing this, Leoni *et al.* [4] carried out a comparative study of various international guidelines for the management of NAFLD, shedding light on both consistencies and discrepancies across different clinical recommendations.

Further insight into clinical perspectives was provided by surveys conducted by Nadolsky *et al.* [5] and Sebastiani *et al.* [6], which explored the attitudes and understanding of both patients and physicians regarding the diagnosis and treatment of non-alcoholic steatohepatitis (NASH). These investigations revealed ongoing challenges and

knowledge gaps in NAFLD management among medical professionals and their patients.

A secondary aim of the present research is to evaluate the awareness and opinions of pharmacy students regarding the role of metformin in treating NAFLD—a topic on which limited literature exists. One related effort is the Canadian survey by Sebastiani *et al.* [6], which, although not focused solely on metformin, offers relevant insights into the general understanding of NAFLD among healthcare providers. This survey, targeting hepatologists and nephrologists, revealed a reasonable level of familiarity with NAFLD but also identified several key knowledge deficits, including inconsistencies in diagnostic strategies and limited understanding of specific management aspects like liver biopsy use and cardiovascular risk mitigation.

In addition, Nadolsky *et al.* [5] carried out a study examining both patient and primary care physician perspectives on the diagnosis and treatment of non-alcoholic steatohepatitis (NASH), which may indirectly reflect opinions on the potential use of metformin as a therapeutic option. The research shed light on widespread knowledge gaps among both groups. Patients were often unfamiliar with the disease and expressed concerns related to social stigma and the side effects of medications. On the other hand, primary care physicians reported limited confidence in diagnosing and managing NASH, and there was little agreement on preferred treatment strategies.

Specific to metformin, the findings indicated a lack of consensus among healthcare providers about its role in treating NASH. This uncertainty underscores the need for further evidence and clinical guidance concerning the drug's efficacy in this setting. The study emphasized the importance of enhanced educational efforts and clearer clinical protocols to strengthen both patient understanding and physician competence in addressing NASH.

Overall, the current study aims to provide a detailed examination of metformin's therapeutic potential in managing NAFLD. In parallel, it investigates the knowledge and perspectives of pharmacy students regarding NAFLD and the possible application of metformin as part of its treatment. These insights are intended to guide future curriculum development and promote the integration of NAFLD-related content into pharmaceutical education and therapeutic training programs.

Materials and Methods

This investigation involved a group of 41 first-year pharmacy students enrolled at Howard University College of Pharmacy. The survey achieved a high completion rate of 92%, indicating strong participation. The research was embedded as part of the drug informatics coursework. Participants were asked to fill out a structured questionnaire that gathered background information across eight categories, including age, gender, previous education, place of residence before enrollment, employment history, and income bracket. The survey also featured ten main content questions—five assessing factual knowledge and five gauging student opinions—using a five-point Likert scale ranging from strong agreement to strong disagreement. The responses were statistically examined using SPSS software, employing both descriptive methods and chi-square tests to identify significant relationships.

Results and Discussion

A summary of participant demographics (**Table 1**) shows that most respondents were between 18 and 24 years old (76.2%, $n = 32$). Women made up a slight majority at 54.8% ($n = 23$). Just under half of the students (47.6%, $n = 20$) had relocated from outside the DMV (District of Columbia, Maryland, and Virginia) area, indicating a varied geographic distribution among participants. Educationally, a significant number (69%, $n = 29$) had already earned an undergraduate degree such as a BA or BS before entering the program, highlighting a relatively advanced academic background within the group.

Table 1. Demographics of participants

Demographics	Group	N (%)
Age	18-24 years	32 (76.2)
	35 years and older	7 (16.7)
Gender	Female	23 (54.8)
	Male	16 (38.1)
Residence	Washington DC	2 (4.8)
	Maryland	10 (23.8)
	Virginia	7 (16.7)
	Other states	20 (47.6)
Education	Some college	4 (9.5)
	2nd-year degree	3 (7.1)
	4-year degree	29 (69.0)
	Professional degree	3 (7.1)

Table 2 highlights the key characteristics of the study participants concerning their professional and economic backgrounds. A notable 31.0% ($n = 13$) of the respondents are employed in pharmacy-related fields. Regarding income, 28.6% ($n = 12$) of the participants reported earnings under \$10,000 annually. Employment status shows that the majority, 81.0% ($n = 34$), are employed full-time. Additionally, nearly half of the participants (45.2%, $n = 19$) have accumulated 1-3 years of experience in their respective fields, indicating a reasonable level of professional background within the sample group.

Table 2. Professional, income, and employment experience overview

Demographics	Group	N (%)
Job Type	Non-pharmacy or non-healthcare	8 (19.0)
	Pharmacy-related	13 (31.0)
	Non-pharmacy but healthcare-related	12 (28.6)
	Not Applicable	9 (21.4)
Annual Income	< \$10,000	12 (28.6)
	\$10,000-\$19,999	2 (4.8)
	\$20,000-\$29,999	5 (11.9)
	\$30,000-\$39,999	7 (16.7)
	\$40,000-\$49,999	4 (9.5)
Work Experience	> \$49,999	6 (14.3)
	Employed	34 (81.0)
	Never worked	5 (11.9)
Years Worked	< 1 year	3 (7.1)
	1-3 years	19 (45.2)
	4-5 years	2 (4.8)
	> 5 years	11 (26.2)

The following two tables explore how different age groups impact the understanding of metformin's role in managing NAFLD. They specifically address the relationship between age and familiarity with metformin as a treatment for this liver condition.

As seen in **Table 3**, the study examines how participants' familiarity with metformin in the context of NAFLD varies by age. Younger participants, specifically those aged 18-24, show higher levels of awareness compared to older individuals. This trend is reflected across multiple factors, including knowledge of FDA-approved drugs for NAFLD, support for using non-FDA-approved drugs like metformin, and familiarity with the stages of NAFLD and its treatments. Additionally, differences in

understanding the forms and dosages of metformin used for diabetes management are also notable. These findings suggest that age-related differences must be considered

when addressing gaps in knowledge about metformin's application in NAFLD care and treatment strategies.

Table 3. Age group comparison in familiarity with metformin use in NAFLD ($P < 0.05$)

Survey question (Likert scale)	Age 18-24 (n = 32, 76.2%)	Age > 35 (n = 7, 16.7%)	Agree/strongly agree	Disagree/strongly disagree
1. Familiarity with metformin's role in NAFLD management	17 (45.9%)	4 (10.8%)	13 (35.1%)	3 (8.1%)
2. Unfamiliar with any FDA-approved drugs to reverse fatty liver disease	8 (21.6%)	3 (8.1%)	22 (59.4%)	4 (10.8%)
3. Metformin is non-FDA-approved for NAFLD, so it's not recommended	14 (37.8%)	2 (5.4%)	16 (43.2%)	5 (13.5%)
4. Metformin may be beneficial for NAFLD	8 (21.6%)	4 (10.8%)	22 (59.5%)	3 (8.1%)
5. Belief in FDA-approved drugs for NAFLD	5 (13.5%)	1 (2.7%)	25 (67.6%)	6 (16.2%)
6. Awareness of the four stages of NAFLD, with most cases detected early	8 (21.6%)	4 (10.8%)	22 (59.5%)	3 (8.1%)
7. Recognizing liver fat accumulation as a key feature of NAFLD	3 (8.1%)	1 (2.7%)	27 (72.9%)	6 (16.2%)
8. Metformin is available in oral tablets and solutions	4 (10.8%)	0 (0%)	26 (70.2%)	7 (18.9%)
9. Fibrosis occurs with persistent liver inflammation causing scars	10 (27.0%)	3 (8.1%)	20 (54.0%)	4 (10.8%)
10. Metformin, exercise, and a healthy diet are used to manage high blood sugar	7 (18.9%)	0 (0%)	23 (62.1%)	7 (18.9%)

Table 4 highlights the relationship between gender and knowledge of metformin's use in the treatment of NAFLD. The results reveal that females exhibit a higher level of familiarity with metformin's role in NAFLD management compared to males. Conversely, males show greater awareness of FDA-approved medications for reversing fatty liver disease. Females are also more likely to recommend metformin, a non-FDA-approved treatment for NAFLD, in comparison to males. Additionally, females have a better understanding of how

liver inflammation and scarring affect nearby blood vessels. Lastly, females are more inclined to agree that combining metformin with a healthy lifestyle, including exercise and diet, is effective for managing high blood sugar levels. These gender-based differences in familiarity and attitudes highlight the importance of considering gender-specific approaches when addressing knowledge gaps and designing educational programs for metformin use in NAFLD management.

Table 4. Gender comparison in knowledge of metformin for NAFLD ($P < 0.05$)

Question	Survey questions (Likert scale)	Agree/strongly agree	Disagree/strongly disagree
		Males (n = 9)	Females (n = 23)
1	Familiarity with metformin for managing NAFLD	5 (13.5%)	16 (43.2%)
2	Lack of familiarity with FDA drugs for reversing fatty liver disease	5 (13.5%)	16 (43.2%)
3	Reluctance to recommend metformin (non-FDA-approved) for NAFLD	4 (10.8%)	12 (32.4%)
4	Perception that metformin could be beneficial for NAFLD	3 (8.1%)	9 (16.2%)
9	Awareness of fibrosis due to inflammation and scarring in the liver	3 (8.1%)	10 (27.0%)
10	Agreement that metformin, exercise, and a healthy diet help manage high blood sugar	6 (16.2%)	6 (16.2%)

Table 5 illustrates the connection between employment status and familiarity with metformin's role in NAFLD management. The findings indicate that employed

participants show a higher level of agreement regarding their awareness of metformin for treating NAFLD compared to those who are unemployed. Additionally,

employed individuals are more likely to recommend metformin and exhibit a better understanding of the relationship between liver inflammation, scarring, and blood vessels. Finally, employed participants are more

inclined to agree that the combination of metformin, exercise, and diet is effective for managing high blood sugar levels.

Table 5. Employment status and familiarity with metformin for NAFLD ($P < 0.05$)

Question	Survey questions (Likert scale)	Agree/strongly agree	Disagree/strongly disagree
		Employed (n = 37)	Unemployed (n = 5)
1	Familiar with metformin for managing NAFLD	17 (45.9%)	4 (10.8%)
2	Unfamiliar with any effective FDA drugs for reversing fatty liver disease	10 (27.0%)	1 (2.7%)
3	Metformin is a non-FDA-approved drug, so I wouldn't recommend it	13 (35.1%)	3 (8.1%)
4	Metformin seems beneficial for NAFLD	10 (27.0%)	2 (5.4%)
5	There are FDA-approved drugs for NAFLD	4 (10.8%)	2 (5.4%)
6	NAFLD develops in stages, mostly detected in the first phase	9 (24.3%)	3 (8.1%)
7	The main characteristic of NAFLD is excess fat in the liver cells	4 (10.8%)	0 (0%)
8	Metformin is available in oral tablets and solutions	4 (10.8%)	0 (0%)
9	Fibrosis does not occur when inflammation persists and causes scarring in the liver and blood vessels	11 (29.7%)	2 (5.4%)
10	Metformin, combined with exercise and a healthy diet, is used to manage high blood sugar levels	7 (18.9%)	0 (0%)

Table 6 presents findings on how individuals' residency status influences their understanding of metformin's use for managing NAFLD. Notably, employed individuals from other states show greater familiarity with metformin for NAFLD management than their peers from Washington, Maryland, or Virginia. These individuals are also more likely to recommend metformin, despite its non-FDA approval. Additionally, those employed in other states have a more comprehensive understanding of the relationship between liver inflammation, scarring, and blood vessels. Moreover, individuals from other states show more support for using metformin alongside exercise and a healthy diet to manage high blood sugar levels. These regional differences highlight the importance of tailoring educational interventions based on geographic factors to enhance their effectiveness.

Table 6 highlights the influence of geographical location on participants' awareness of metformin's role in treating NAFLD. Respondents living outside the DMV area (D.C., Maryland, Virginia) appear to have a higher level of knowledge about metformin and its potential use in NAFLD management. Those residing outside of the DMV region are also more inclined to suggest metformin, despite it being a non-FDA-approved treatment for NAFLD. Furthermore, these participants show a greater understanding of the connection between liver inflammation, fibrosis, and blood vessels compared to their DMV counterparts. The findings suggest that location could be a factor influencing individuals' perceptions and knowledge of NAFLD treatment options.

Table 6. Residency (state) and knowledge of metformin for NAFLD ($P < 0.05$)

Survey question	Agree/strongly agree	Disagree/strongly disagree	DMV (n = 37)	Other States (n = 15)	DMV (n = 37)	Other states (n = 15)
1	Knowledge of metformin for NAFLD treatment	10 (27.0%)	10 (27.0%)	12 (32.4%)	9 (24.3%)	
2	Unaware of any FDA drugs to reverse fatty liver	6 (16.2%)	5 (13.5%)	12 (32.4%)	14 (37.8%)	

3	Would not recommend metformin as it is not FDA-approved	8 (21.6%)	8 (21.6%)	10 (27.0%)	11 (29.7%)
4	Believes metformin has potential for NAFLD treatment	6 (16.2%)	6 (16.2%)	10 (27.0%)	13 (35.1%)
5	Believes there are FDA-approved treatments for NAFLD	3 (8.1%)	3 (8.1%)	15 (40.5%)	16 (43.2%)
6	NAFLD progresses in stages, with early detection in the first phase	5 (13.5%)	7 (18.9%)	13 (35.1%)	12 (32.4%)
7	NAFLD is characterized by fat buildup in the liver	2 (5.4%)	2 (5.4%)	16 (43.2%)	17 (45.9%)
8	Metformin is available in oral tablet and solution forms	8 (21.6%)	3 (8.1%)	8 (21.6%)	16 (43.2%)
9	Fibrosis develops from persistent inflammation and liver scarring	8 (21.6%)	5 (13.5%)	10 (27.0%)	14 (37.8%)
10	Metformin, combined with exercise and a healthy diet, helps manage high blood sugar	2 (5.4%)	5 (13.5%)	14 (37.8%)	14 (37.8%)

Table 7 examines the connection between education level and participants' familiarity with metformin for NAFLD management. Individuals with a four-year degree demonstrate significantly more knowledge about metformin and its application for NAFLD than those with less education, including those with some college or a professional degree. Furthermore, those with a four-year degree are more likely to recommend metformin and

have a deeper understanding of how liver inflammation and scarring contribute to NAFLD. Additionally, participants with a four-year degree show stronger support for the combined use of metformin, exercise, and a healthy diet in managing high blood sugar levels. These findings suggest that educational interventions should be tailored to address the specific knowledge gaps based on individuals' educational backgrounds.

Table 7. Relationship between education level and familiarity with metformin in NAFLD

Survey question	Some, 2-year, or professional degree	4-year degree
1. Familiar with metformin's role in managing NAFLD (P-value = 0.001)	17% (4)	11% (5)
2. Not familiar with FDA-approved drugs for reversing fatty liver (P-value = 0.002)	8% (3)	20% (4)
3. Would not recommend metformin, as it's non-FDA-approved (P-value = 0.006)	12% (4)	16% (5)
4. Metformin may be beneficial for NAFLD (P-value = 0.002)	9% (3)	19% (5)
5. Believe FDA-approved drugs are available for this condition (P-value = 0.011)	5% (0)	23% (8)
6. NAFLD progresses through four stages, mainly detected early on (P-value = 0.009)	8% (4)	20% (5)
7. Excessive fat accumulation in liver cells is a key NAFLD feature (P-value = 0.001)	3% (1)	25% (8)
8. Fibrosis results from persistent inflammation causing liver scarring (P-value = 0.004)	8% (5)	20% (4)
9. Metformin with exercise and diet helps manage blood sugar levels (P-value = 0.002)	6% (1)	22% (8)

Study objective

This study aims to achieve two main objectives: first, to conduct a review of the literature on the potential use of metformin in treating NAFLD, and second, to analyze student knowledge and opinions on the subject. Metformin has shown the potential to enhance liver function and decrease fat accumulation in NAFLD patients, especially when lifestyle modifications are not enough. Its mechanisms, such as improving insulin sensitivity and reducing liver glucose production, suggest

it could slow NAFLD progression. However, varying levels of knowledge and differing opinions among healthcare professionals highlight the need for more research and focused educational efforts to maximize the benefits of metformin in treating NAFLD.

Survey insights

The survey results suggest significant age-related differences in knowledge about metformin in the context of NAFLD. Participants aged 18-24 years appear to be

notably more familiar with its use, while those in the 24-34 age range displayed little to no awareness. This discrepancy points to potential generational differences in knowledge and attitudes toward NAFLD treatment options.

The analysis highlights key differences in how age groups perceive metformin's role in managing NAFLD. A noticeable trend is that younger participants (18-24 years) are less familiar with FDA-approved drugs for reversing fatty liver disease. Conversely, there is a statistically significant difference between those aged 18-24 years and those 35 years and older in terms of their willingness to recommend metformin, a non-FDA-approved treatment for NAFLD. Further, the understanding of NAFLD stages varies significantly across age groups, with younger participants demonstrating a stronger grasp of treatment options for the condition. Additionally, familiarity with the various forms of metformin shows significant variation depending on age, as does awareness of its use in diabetes management, underscoring the need for age-targeted educational efforts to close these knowledge gaps.

Gender differences also stand out in terms of metformin familiarity. Females exhibit a higher level of awareness regarding metformin's role in managing NAFLD compared to males, while males are more knowledgeable about FDA-approved drugs for the condition. Females are more inclined to recommend metformin for NAFLD despite its non-FDA approval, and they also show a deeper understanding of the relationship between fibrosis and liver tissue damage.

Educational background plays a crucial role in understanding metformin's potential in treating NAFLD. Those with a 4-year degree show a higher degree of familiarity with metformin's benefits in NAFLD management and are more likely to recommend it. This suggests that higher education is closely tied to a deeper understanding of medical treatments like metformin. Meanwhile, work experience had a more modest impact on metformin familiarity, although individuals from healthcare-related fields (excluding pharmacy) displayed a better grasp of the drug's role in managing NAFLD. Interestingly, prior work experience did influence the likelihood of recommending metformin, indicating that professional background can shape opinions on treatment options.

These findings emphasize the importance of tailoring educational strategies to account for factors like age, gender, educational level, and professional experience in

enhancing awareness and understanding of metformin's applications in managing NAFLD.

Gender-based differences in familiarity with metformin for NAFLD management

The analysis reveals that females tend to express stronger agreement with the use of metformin, combined with exercise and a healthy diet, for managing high blood sugar levels compared to males. This difference may stem from factors like variations in health behaviors between genders, targeted health initiatives, or differing medical advice from healthcare providers. These gender distinctions emphasize the need for more targeted educational approaches to bridge knowledge gaps about metformin's role in NAFLD management.

Study limitations

The study's sample, consisting of 41 first-year pharmacy students from Howard University College of Pharmacy, may limit the applicability of the results to broader populations. Expanding the sample size and including diverse groups would offer a more representative view of public and healthcare professional knowledge regarding metformin and NAFLD. The study also has a self-report bias, as participants' responses may be influenced by social desirability or misunderstanding of the questions, potentially distorting the results. Additionally, the focus on first-year pharmacy students restricts the generalizability to a wider array of healthcare providers or NAFLD patients. Including these groups in future research could provide a more holistic understanding. Since the study was cross-sectional, it cannot infer causality or examine changes over time. Longitudinal studies could offer more detailed insights into how knowledge and opinions evolve. Lastly, the wording and structure of the Likert scale in the questionnaire may have influenced the way participants responded. Refining the survey could help enhance the accuracy and reliability of the findings.

Conclusion

This study provides valuable insights into the understanding and opinions of first-year pharmacy students regarding metformin in the treatment of NAFLD. It shows that age, gender, employment status, and geographic location (residency) significantly influence familiarity with metformin. Younger students exhibited greater awareness, and females were more likely to recommend the drug. Employment and

residency status also played a role in awareness levels, with employed individuals and those from certain regions showing higher familiarity. These findings highlight the need for tailored educational programs that address the specific needs and knowledge gaps of different demographic groups to improve understanding and application of metformin in NAFLD management.

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