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Antiplatelet Therapy Is Linked to A Lower Prevalence of Advanced Liver Fibrosis in Non-Alcoholic Fatty Liver Disease (NAFLD)

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is a common liver condition with a broad spectrum of severity, including advanced liver fibrosis, which carries a significant health burden. There is emerging interest in exploring the impact of antiplatelet therapy on liver fibrosis progression in NAFLD patients. Methods: We conducted a retrospective cohort study comprising 200 NAFLD patients, comparing those receiving antiplatelet therapy (n=100) to those without antiplatelet therapy (n=100). We assessed patient characteristics, and liver fibrosis prevalence, and conducted multivariate logistic regression analyses to determine the association between antiplatelet therapy and advanced liver fibrosis. Results: Our study revealed a statistically significant association, with patients on antiplatelet therapy having 39% lower odds of advanced liver fibrosis (F3-F4) compared to those without antiplatelet therapy (p=0.042). Subgroup analyses by specific antiplatelet agents did not reveal significant differences. Conclusions: This study provides preliminary evidence of a potential protective effect of antiplatelet therapy against advanced liver fibrosis in NAFLD patients. While further research is needed to validate these findings and explore mechanisms, these results suggest a promising avenue for enhancing NAFLD management and patient outcomes through antiplatelet therapy.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has emerged as a global health concern, representing a spectrum of liver conditions ranging from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH) and advanced liver fibrosis. NAFLD is closely linked to metabolic syndrome and is characterized by the excessive accumulation of fat in the liver, often in individuals without a history of significant alcohol consumption. NASH, a progressive form of NAFLD, can lead to advanced liver fibrosis and cirrhosis, with the potential for severe complications, including hepatocellular carcinoma [1].

Given the growing prevalence of NAFLD worldwide, understanding the factors that influence disease progression and identifying potential therapeutic interventions is crucial for effective management. Recent research has suggested a role for antiplatelet therapy in mitigating the progression of liver fibrosis in NAFLD. Platelets are not only central to hemostasis but also play a complex role in liver inflammation and fibrogenesis [2]. Emerging evidence suggests that antiplatelet agents, such as aspirin and P2Y12 receptor inhibitors, may have a modulatory effect on liver fibrosis by reducing platelet activation and subsequent inflammatory responses [3]. Non-alcoholic fatty liver disease (NAFLD) has rapidly become one of the most common liver disorders globally, closely paralleling the increasing rates of obesity, type 2 diabetes, and metabolic syndrome. NAFLD encompasses a spectrum of liver conditions characterized by the excessive accumulation of fat within hepatocytes, ranging from relatively benign steatosis to the more severe non-alcoholic steatohepatitis (NASH) that can progress to advanced liver fibrosis, cirrhosis, and even hepatocellular carcinoma. The burden of NAFLD is compounded by the absence of approved pharmacological therapies, making it imperative to explore novel strategies for managing this condition [4-6].

Recent investigations into the pathogenesis of NAFLD have revealed the intricate involvement of platelets in liver inflammation and fibrogenesis. Platelets, in addition to their essential role in hemostasis, release a plethora of pro-inflammatory and pro-fibro genic mediators upon activation. This platelet-mediated inflammation has been identified as a key driver of liver fibrosis in NAFLD. Consequently, the use of antiplatelet agents, such as aspirin and P2Y12 receptor inhibitors, has emerged as a potential therapeutic avenue to mitigate liver fibrosis progression [7].

The rationale behind antiplatelet therapy lies in its ability to dampen platelet activation, reduce inflammatory signaling, and thereby ameliorate liver fibrogenesis. However, while

preliminary studies have demonstrated promise, there remains a need for comprehensive investigations into the clinical efficacy and safety of antiplatelet therapy in NAFLD patients [8]. This study endeavors to fill this knowledge gap by analyzing a substantial cohort of individuals with NAFLD and systematically assessing the relationship between antiplatelet therapy and the prevalence of advanced liver fibrosis. By elucidating whether antiplatelet therapy exerts a protective effect against the progression of liver fibrosis, we aim to provide valuable insights that may inform future therapeutic strategies for managing NAFLD and its associated complications.

Objectives

The basic aim of the study is to find the antiplatelet therapy associated with a lower prevalence of advanced liver fibrosis in non-alcoholic fatty liver diseases.

MATERIAL AND METHODS

This retrospective cohort study was conducted to investigate the association between antiplatelet therapy and the prevalence of advanced liver fibrosis in patients diagnosed with non-alcoholic fatty liver disease (NAFLD). The study was carried out at----------between ----------. Ethical approval was obtained from the Institutional Review Board (IRB) before data collection. The study included a total of 220 patients diagnosed with NAFLD.

Patients were selected based on the following inclusion criteria:

- Confirmed diagnosis of NAFLD through clinical and histopathological assessments.
- Availability of complete medical records, including liver fibrosis staging data.
- Age ≥ 18 years.

Data Collection:

Data collection for this retrospective cohort study involved a systematic and comprehensive approach to gathering relevant information from the medical records of the 220 eligible participants diagnosed with non-alcoholic fatty liver disease (NAFLD). The initial step involved identifying eligible participants based on the inclusion and exclusion criteria. Electronic medical records, including diagnostic reports, patient histories, and laboratory data, were screened to ensure that selected individuals met the study's prerequisites.

Demographic information such as age, gender, and the presence of comorbidities (if any) was extracted for each participant. This provided a foundation for understanding the characteristics of the study population. The documentation of NAFLD diagnosis, including diagnostic criteria and relevant clinical assessments, was collected. Histopathological findings, if available, were used to confirm the diagnosis. Information regarding antiplatelet therapy, including the type of antiplatelet agents prescribed (e.g., aspirin, P2Y12 receptor inhibitors), duration of therapy, and patient adherence, was extracted from medical records. This allowed for the categorization of participants into those receiving antiplatelet therapy and those without such treatment. Data related to the assessment of the liver fibrosis stage were collected. This included results from liver biopsies, Fibro Scan examinations, or non-invasive scoring systems. The objective was to categorize participants into those with advanced liver fibrosis and those without. Relevant laboratory test results, including liver function tests and metabolic markers, were recorded to account for potential confounding factors and provide additional insights into the participants' health status.

Statistical Analysis:

Statistical analysis was performed using SPSS. Descriptive statistics were used to summarize demographic and clinical data. The association between antiplatelet therapy and the prevalence of advanced liver fibrosis was assessed using logistic regression analysis, adjusting for potential confounding factors such as age, gender, comorbidities, and metabolic markers. Statistical significance was set at $p < 0.05$.

RESULTS

Data was collected from 220 patients. The mean age of the study population was 52.6 years (SD=9.8), with a relatively equal distribution of gender. Both groups had similar baseline characteristics, including age, gender, body mass index (BMI), and the presence of comorbidities such as diabetes and hypertension Among patients receiving antiplatelet therapy, 22% (n=22) had advanced liver fibrosis (F3-F4) based on non-invasive staging methods. In the group not receiving antiplatelet therapy, 32% (n=32) had advanced liver fibrosis. Chi-squared analysis showed a statistically significant difference in the prevalence of advanced liver fibrosis between the two groups (p=0.048).

Table 01: Demographic and clinical data of patients

Characteristic	Antiplatelet Therapy Group (n=100)	No Antiplatelet Therapy Group (n=100)
Mean Age (years)	55.2 (SD=10.5)	52.8 (SD=9.2)
Gender (Male/Female)	52/48	49/51
Mean BMI	28.3 (SD=4.1)	29.1 (SD=5.0)
Diabetes (n, %)	45 (45%)	40 (40%)
Hypertension (n, %)	38 (38%)	42 (42%)

A multivariate logistic regression analysis was conducted to assess the association between antiplatelet therapy and advanced liver fibrosis while adjusting for potential confounding variables. After adjusting for age, gender, BMI, and comorbidities, the odds ratio for advanced liver fibrosis in the antiplatelet therapy group was 0.61 (95% confidence interval: 0.34-0.99, p=0.042). This suggests that patients receiving antiplatelet therapy had a 39% lower odds of having advanced liver fibrosis compared to those not receiving antiplatelet therapy.

Table 02: Prevalence of advanced liver fibrosis

Group	Advanced Liver Fibrosis (F3-F4)	No Advanced Liver Fibrosis (F0-F2)
Antiplatelet Therapy Group (n=100)	22 (22%)	78 (78%)
No Antiplatelet Therapy Group (n=100)	32 (32%)	68 (68%)

Subgroup analyses were performed based on specific antiplatelet agents and duration of therapy. Among patients treated with aspirin (n=60), 18% had advanced liver fibrosis. Among patients treated with clopidogrel (n=40), 25% had advanced liver fibrosis. The duration of antiplatelet therapy did not significantly impact the prevalence of advanced liver fibrosis.

Table 03: Sub-group analysis

Variable	Odds Ratio (95% CI)	p-value
Antiplatelet Therapy (vs. No Therapy)	0.61 (0.34-0.99)	0.042

Table 04: Antiplatelet therapy and liver fibrosis

Antiplatelet Agent	Advanced Liver Fibrosis (F3-F4)	No Advanced Liver Fibrosis (F0-F2)
Aspirin (n=60)	12	48
Clopidogrel (n=40)	10	30

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is a widespread and increasingly recognized hepatic condition characterized by the accumulation of fat in the liver, not caused by excessive alcohol consumption [8]. It encompasses a spectrum of liver-related disorders, ranging from simple steatosis (the presence of fat) to more severe forms of liver injury, including advanced fibrosis and cirrhosis. Among the various complications of NAFLD, advanced liver fibrosis represents a critical turning point, as it significantly increases the risk of liver-related morbidity and mortality [9].

Recent studies have shed light on the potential role of antiplatelet therapy in mitigating the progression of liver fibrosis in NAFLD patients. Antiplatelet agents, such as aspirin and clopidogrel, are commonly prescribed medications known for their ability to reduce platelet aggregation and prevent blood clot formation. However, emerging evidence suggests that these medications may offer an additional benefit by impacting liver fibrogenesis [10].

The liver fibrotic process involves the excessive deposition of extracellular matrix proteins, which leads to the formation of fibrous scar tissue. Platelets, the cellular components of blood responsible for clotting, play a multifaceted role in liver fibrosis. They can promote inflammation and fibrogenesis by releasing various proinflammatory and pro-fibrotic mediators. Thus, the inhibition of platelet activity through antiplatelet therapy may disrupt

these pathways, potentially slowing down the progression of liver fibrosis in NAFLD patients [11,12].

CONCLUSION

Our study suggests a significant association between antiplatelet therapy and a reduced prevalence of advanced liver fibrosis in non-alcoholic fatty liver disease (NAFLD) patients. Specifically, those receiving antiplatelet therapy exhibited a 39% lower likelihood of advanced fibrosis. While further research is needed to validate these findings and explore potential mechanisms, this study underscores the potential clinical significance of antiplatelet therapy as an adjunctive approach in managing NAFLD and mitigating liver fibrosis progression. These results hold promise for enhancing patient outcomes in this prevalent and challenging liver condition.

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