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The Effect of Smoking Habits on Decreased Liver Function in Active Smokers Aged 20–50 Years old

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Abstract

Background : AA study was conducted to determine the effect of smoking habits on decreased liver function in active smokers aged 20–50 years. This study was motivated by Indonesia's high smoking prevalence and its associated liver-related health issues. The liver is an organ that plays a role in the body's metabolism. Smoking triggers the formation of free radicals, causing a decrease in liver function and inflammation.
Methods : In this study, mix method design was used with active smokers as the smoker group and the control group was respondents not active or passive smokers. Groups are categorized again based on age, ie 20–30, 31–40, and 41–50. The study population is the academic community of the Hermina Health Institute Jatinegara Campus and the community living on Kapitan III Road Tapos District, Depok City. Liver function is evaluated through enzymes SGPT, SGOT, ALP, and CRP as parameters for inflammation. To evaluate the influence of smoking habits and lifestyle factors on liver function risk, an analysis of variance (ANOVA) followed by post-hoc testing and linear regression analysis were performed.
Results : Laboratory results showed that mean levels of ALT, AST, ALP, and CRP were higher in the smoker group compared to controls across all age categories, although most values remained within normal limits. ANOVA revealed statistically significant differences in all biomarkers (p<0.05), and post-hoc tests identified specific age-related group differences. Smokers' habit data indicated that most smokers began smoking between the ages of 1520 and had smoked for over five years. Lifestyle analysis showed a higher prevalence of insufficient physical activity, reduced sleep duration, and higher BMI among smokers. CLDQ scores for both groups generally reported minimal emotional disturbance and no signs of advanced liver disease.
Conclusion : Smoking is associated with elevated liver enzymes (ALT, AST, ALP) and CRP levels, indicating subclinical hepatic and inflammatory alterations. These biochemical changes correlate with lifestyle risk factors and diminished quality of life. Early screening and lifestyle modification are recommended to prevent long-term hepatic damage among smokers.

Keywords : Active smokers, inflammatory event, liver enzymes, productive age, smoking

INTRODUCTION

A wide array of health complications has been linked to habitual tobacco use. According to the World Health Organization (WHO), as of 2023, tobacco smoking contributes to approximately 8 million deaths globally each year, with 1.3 million of these attributed to secondhand smoke exposure.[1] In Indonesia, WHO data from 2020 reported an estimated 225,700 deaths annually due to smoking and other tobacco-related illnesses. Furthermore, the prevalence of active smoking among Indonesian adolescents aged 1019 has shown an alarming increase, rising from 7.2% in 2013 to 9.1% in 2018.[2] The unregulated sale of cigarettes, particularly the lack of age restrictions, significantly hampers tobacco control efforts and exacerbates public health risks.

Cigarettes contain a multitude of toxic compounds, including tar, nicotine, and carbon monoxide, which adversely affect both active smokers and those exposed to secondhand smoke.[3] Additionally, the presence of heavy metals in cigarettes––whether traditional or electronic––poses a substantial threat to human health, primarily through the induction of oxidative stress and systemic inflammation.[4] Cigarette smoke exposure triggers cellular inflammation, which, if unmitigated, may progress to chronic conditions resulting in metabolic syndromes and extensive organ damage.[5]

A 2021 study by Premkumar and Anand highlighted that tobacco consumption can accelerate the oxidation of Nicotinamide Adenine Dinucleotide Phosphate (NADPH), disrupting the body's antioxidant defense mechanisms and promoting free radical formation. This oxidative imbalance contributes to hepatocyte inflammation, cellular injury, fibrotic mediator proliferation, and hepatic iron accumulation. Smoking has also been linked to vascular constriction, endothelial dysfunction, tissue hypoxia, and hepatocellular damage.[6]

Moreover, tobacco smoke is a rich source of free radicals and heavy metals, which provoke oxidative stress and persistent inflammation.[7] Chronic exposure to these radicals significantly elevates the risk of organ impairment.[6] The liver, as a central organ in detoxification and immune response, is particularly vulnerable. Prolonged smoking leads to the accumulation of reactive oxygen species (ROS), which stimulates the production of pro-inflammatory cytokines such as IL-6 and TNF-α. These cytokines subsequently induce hepatic synthesis of C-reactive protein (CRP), resulting in elevated systemic CRP levels. Persistent inflammation, if left uncontrolled, can compromise hepatic function, as reflected in the increased serum levels of liver enzymes including ALT, AST, and ALP.[8,9]

The progression from inflammation to hepatic injury is closely associated with the cumulative effect of oxidative stress, which is influenced by both the quantity of cigarettes consumed daily and the duration of smoking. In addition to smoking, several lifestyle-related risk factors contribute to liver dysfunction, such as frequent consumption of high-fat foods, alcohol intake, physical inactivity, and inadequate rest. These behaviors are often linked to elevated body mass index (BMI), which in turn heightens the risk of hepatic steatosis, non-alcoholic fatty liver disease (NAFLD), and cirrhosis.[10,11]

Although previous studies have explored the association between smoking and the elevation of inflammatory biomarkers and liver enzymes, comprehensive analyses examining the interplay between smoking and additional risk factors remain scarce. The present study aims to investigate the cumulative impact of smoking habitsincluding smoking duration, frequency, and the age at smoking initiationon hepatic function. It further considers non-smoking lifestyle factors such as alcohol use, sleep duration, and physical activity. Participants in this study are restricted to adults aged 2050 years to specifically evaluate the effects of smoking within the productive age range. Individuals over 50 were excluded to minimize confounding factors associated with age-related organ function decline.

The working hypothesis of this study posits that predefined risk factors––particularly active smoking––are significantly associated with impaired hepatic function, as evidenced by elevated inflammatory biomarkers and liver enzyme levels in the smoker group compared to non-smokers.

METHODS

Research Design and Variables

This study employed a mixed-methods approach, integrating both qualitative and quantitative methodologies within an experimental research design to investigate the causal relationship between independent and dependent variables using liver and inflammation biomarker, and we conducted an investigation into lifestyle habits using a questionnaire filled out by means of direct interviews with all respondents. The independent variables comprised smoking-related behaviors––including active smoking status, age at smoking initiation, smoking duration, and the number of cigarettes consumed per day––as well as lifestyle factors such as alcohol consumption, physical activity, sleep duration, and body mass index (BMI). The dependent variables were selected biomarkers indicative of hepatic function and systemic inflammation: C-reactive protein (CRP), alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP).

Participants were divided into two groups: the control group, consisting of individuals who neither

smoked nor lived in environments with active smokers, and the experimental group, consisting of active smokers observed for this study. Confidentiality and anonymity of all respondents were strictly maintained; no names, initials, or complete addresses were recorded or disclosed.

The study sample included individuals aged 20 to 50 years, further classified into three age-based subgroups for comparative analysis: Group 1 (20–30 years), Group 2 (31–40 years), and Group 3 (41–50 years). These categories were designed to evaluate potential age-related differences in the impact of smoking and associated lifestyle factors on liver function biomarkers.

Population and Sampling

Sampling for this study was conducted using a purposive sampling technique, based on the following inclusion criteria:

1. Age between 20 and 50 years.
2. Non-obese individuals.
3. Free from comorbid conditions such as hepatitis, cirrhosis, or liver cancer.
4. Control group: Non-smokers who do not live with or are not regularly exposed to active smokers.
5. Experimental group: Active smokers who have been smoking for at least one year.

The sample size was calculated using Slovin's formula

$$n = \frac{N}{1 + N(e)^2}$$

Where n is the required sample size, N is the population size, and e is the margin of error. With a 10% margin of error and a total population of 1,200 across the two study sites, the minimum sample size was determined to be 92. This number was increased to 102 participants to account for potential deviations associated with the selected error tolerance.

A 10% margin of error was chosen due to the large population size and the difficulty in finding control participants who are completely free from passive smoke exposure (i.e., not exposed to cigarette smoke for more than one hour per day). This level of tolerance is considered acceptable, as the potential variance between the sample and the population is expected to be minimal.

To obtain data on respondents' smoking habits and lifestyle factors, both structured interviews and questionnaire administration were conducted. The questionnaire comprised 14 items on lifestyle history and 29 items related to chronic liver disease, based on the *Chronic Liver Disease Questionnaire* (CLDQ). Reliability testing of the questionnaire was performed using Cronbach's Alpha, and validity was assessed via Pearson's correlation test

Research Location and Duration

The study was conducted over a one-month period from May to June 2024, across two research sites: Babakan Village, Tapos District, Depok City, and the Hermina Health Institute campus. Ethical clearance for the study was obtained from the Ethics Review Board of Binawan University, with approval number 120/KEPK-UBN/VI/2024.

Blood sample collection was performed immediately following participant interviews and questionnaire completion. Blood was drawn into plain evacuated tubes and stored in a sample collection box before being transported to the laboratory for serum preparation. Biochemical analysis of serum levels––specifically SGPT (ALT), SGOT (AST), ALP, and CRP––was conducted at the Clinical Pathology Laboratory of the Hermina Health Institute, Jatinegara Campus.

Data Analysis

The data analysis procedure began with reliability and validity testing of the questionnaire. Normality and homogeneity of the data were assessed using the Kolmogorov-Smirnov and Levene's tests, respectively. To evaluate the influence of smoking habits and lifestyle factors on liver function risk, analysis of variance (ANOVA) followed by post-hoc testing and linear regression analysis were conducted using IBM SPSS version 26.0. These tests aimed to determine statistically significant differences between independent variables and liver function biomarkers. To estimate the probability and strength of association between risk factors and hepatic impairment, linear regression analysis was employed.

RESULTS

This research employed a mixed-methods approach, incorporating both qualitative and quantitative data collection techniques. Primary data was obtained through direct interviews, self-administered questionnaires, and blood specimen collection, which were subsequently analyzed to assess hepatic function and inflammatory biomarkers.

Participants were restricted to individuals aged 20 to 50 years, with no gender-based exclusion criteria applied. The total respondents in this study were 102 people consisting of 50 control respondents spread across 16 people in the 20–30 year group, 17 people in the 31–40 year group, and 17 people in the 41–50 year group. While the total respondents in the smoker group were 52 people consisting of 19 people in the 20–30 year group, 17 people in the 30–40 year group, and 16 people in the 41–50 year group.

TABLE 1
Laboratory Results of Liver Function Parameters and Inflammatory Marker by Age Group

Age Category	Control		Smoker	
	Mean	SD	Mean	SD
ALT (normal value : ≤ 34 U/L)*				
20–30 years old	15.94	6.81	25.42	8.88
31–40 years old	20.18	8.38	33.18	6.82
41–50 years old	22.76	8.35	35↑	8.62
AST (normal value : ≤ 31 U/L)*				
20–30 years old	16.19	16.19	16.19	16.19
31–40 years old	7.53	7.53	7.53	7.53
41–50 years old	16.59	16.59	16.59	16.59
ALP (normal value: ≤ 240 U/L)*				
20–30 years old	156.88	156.88	156.88	156.88
31–40 years old	51.55	51.55	51.55	51.55
41–50 years old	140.24	140.24	140.24	140.24
CRP (normal value : ≤ 3 mg/L)*				
20–30 years old	4.86↑	1.58↑	8.71↑	4.78↑
31–40 years old	4.69↑	2.00↑	6.29↑	1.68↑
41–50 years old	11.02↑	7.27↑	9.51↑	4.42↑

Table 1 presents the biochemical results, including liver function parameters––alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP)––as well as the inflammatory biomarker C-reactive protein (CRP).

Alanine aminotransferase (ALT or SGPT) and its isoenzyme aspartate aminotransferase (AST or SGOT) are key enzymes used as primary biomarkers of liver cell damage. They catalyze the transfer of amino groups, playing a vital role in metabolism and ATP production. Normally, small amounts circulate in the blood, but elevated levels indicate hepatocyte injury. [12,13]

Alkaline phosphatase (ALP) is a zinc metalloenzyme produced mainly in bile canaliculi and other tissues like bone and placenta. Increased ALP levels signal cholestasis or bile duct damage, though higher levels are also normal during bone growth in children and adolescents. [12,13]

C-reactive protein (CRP) is an acute-phase inflammatory marker synthesized by hepatocytes. Although CRP is a sensitive indicator of systemic inflammation, it is not organ-specific, as its elevation may result from various inflammatory processes, not solely liver injury. Inflammatory stimuli such as tissue damage activate pro-inflammatory cytokinesIL-6, IL-1β, and TNF-α which in turn stimulate hepatic CRP production. CRP levels typically begin to rise within 6 hours of inflammation and may remain elevated for up to 48 hours, making it a reliable and easily detectable biomarker. [14]

As shown in Table 1, levels of ALT, AST, ALP, and CRP were higher in smokers compared to non-smokers, though most values remained within normal clinical ranges. These findings suggest a potential impact of smoking on liver function and inflammation; however, further analysis is needed to determine whether smoking is the primary cause or if other contributing factors are involved.

In addition to biochemical testing, this study conducted interviews and administered the Chronic Liver Disease Questionnaire (CLDQ) to assess smoking habits, lifestyle factors, and health-related quality of life in individuals with potential liver impairment. Results from the interviews are presented in Tables 2 and 3.

Tables 2 and 3 present the results of interviews conducted with respondents. It is important to note that the reliability of these findings is highly dependent on the honesty of the participants. As shown in Table 3, the

TABLE 2
Smoking Habit Data of the Smoker Group

Categories	Age group		
	20–30 years	31–40 years	41–50 years
Smoking habits	19	17	16
There are family members who smoke	19	17	16
Being in a smoker's environment	19	17	16
Cigarettes smoked per day			
1–10 sticks	12	9	1
11–20 sticks	7	6	5
> 20 sticks	0	2	10
Duration of smoking			
< 1 year	3	0	0
1–5 years	14	0	0
> 5 years	2	17	16
Age of first smoking			
< 15 years old	2	7	3
15–0 years old	17	10	13
> 20 years old	0	0	0

majority of respondents in the smoker group reported having smoked for more than five years. Most of them smoke between 1 to 10 cigarettes per day, and the majority began smoking between the ages of 15 and 20.

Table 3 displays the interview data regarding lifestyle habits that may affect liver function. Behaviors such as smoking, consuming high-calorie foods, lack of physical activity, and insufficient rest can lead to an increase in Body Mass Index (BMI) and elevate the risk of liver disorders, including hepatic steatosis, Non-Alcoholic Fatty Liver Disease (NAFLD), and cirrhosis.[10,11]

In addition to the interviews, this study also utilized a questionnaire instrument based on the Chronic Liver Disease Questionnaire (CLDQ), the results of which are presented in Table 3.

The CLDQ (Chronic Liver Disease Questionnaire) results were subjected to a validation test, which demonstrated that the correlation coefficient (r-calculated) ranged from 0.746 to 0.968, exceeding the critical r-value of 0.162 for a sample size of 102 respondents. Additionally, the *p-value* was less than 0.05, indicating that the CLDQ results are valid. Reliability testing, as presented in Table 3, showed a reliability coefficient greater than 0.8, which reflects a high degree of reliability.

The CLDQ is an instrument designed to assess the quality of life in patients with chronic liver disease, aiming to understand how the condition affects physical, emotional, and social aspects of the patient's life. It consists of 29 questions and utilizes a 7-point Likert scale: 1 = all of the time, 2 = most of the time, 3 = a good bit of the time, 4 = some of the time, 5 = a little of the time, 6 = hardly ever, and 7 = never.

Responses to the CLDQ from the two respondent groups indicate that both the control and smoker groups had an average score of 5 in the abdominal symptoms' domain, suggesting that both groups occasionally experienced abdominal discomfort. However, abdominal symptoms do not necessarily indicate liver dysfunction, and therefore, an analysis of lifestyle habits in both groups is warranted.

In the fatigue domain, differences emerged between the groups. The control group had average responses of 4 and 5, indicating they did not frequently experience debilitating fatigue. In contrast, the smoker group predominantly responded with a score of 3, suggesting frequent fatigue and daytime drowsiness. The majority also reported general weakness and low energy. This level of fatigue likely impacts daily physical activity. For both groups, the average response in the activity domain was 5, suggesting occasional difficulty in performing daily physical tasks.

TABLE 3
Lifestyle factor parameters and Chronic Liver Disease Questionnaire (CLDQ) Analysis

Lifestyle Factor parameters	
Alcohol Consumption	• Most participants in both groups never consumed alcohol. • Smoker group had slightly more individuals with rare alcohol consumption (≥3 months).
Exercise Activites	• Control group: Majority exercise 13x/month or never. • Smoker group: More frequent weekly exercise in younger age group; older groups exercised less or never.
Sleep Duration	• Most participants sleep 5–7 hours/day. • Few participants in either group sleep 8–10 hours/day or <5 hours/day
Body Mass Index (BMI)	• Majority in both groups are within **normal** BMI. • More **overweight** individuals in older age groups, especially in the smoker group.
Chronic Liver Disease Questionnaire (CLDQ) Analysis	
Abdominal Symptoms (α = 0.903)	Slightly higher symptom scores in smokers for bloating, pain, and discomfort.
Fatigue (α = 0.972)	• Control group showed higher mean values for strength and energy. • Smokers reported more drowsiness and tiredness.
Systemic Symptoms (α = 0.926)	• Control group had more dry mouth, itching, and shortness of breath. • Smokers had slightly lower scores on average.
Activity (α = 0.789)	• Control group generally had better activity scores. • Smokers had more trouble with lifting or carrying heavy objects.
Emotional Function (α = 0.932)	• Smokers reported higher levels of irritability and depression. • Control group showed slightly better emotional well-being.
Worry (α = 0.963)	Control group reported more intense worry in all items related to disease progression, family, treatment cost, and transplant.

TABLE 4
Results of ANOVA and Post-Hoc ANOVA Tests

Test	**Parameters**	***P-Value***
ANOVA	ALT	0.000
	AST	0.000
	ALP	0.000
	CRP	0.000

Beyond abdominal symptoms, the CLDQ also evaluates systemic symptoms such as body pain, muscle cramps, dry mouth, and itching. The control group generally reported minimal systemic symptoms, with average scores between 5 and 6. However, among smokers, dry mouth was the most commonly reported symptom.

Additional questions addressed emotional well-being and anxiety levels. Both the control and smoker groups showed similar response patterns, with average scores of 5, indicating that levels of depression and anxiety remained within a manageable range. Overall, no respondents from either group reported symptoms consistent with chronic liver disease.

The statistical test used to determine the effect of smoking habits on liver function and the occurrence of inflammation was a parametric ANOVA with post-hoc analysis. This test was selected based on the results of the normality and homogeneity tests, both of which yielded *p-values* greater than 0.05, indicating that the data met the assumptions required for parametric testing. The results of the ANOVA post-hoc analysis are presented in Table 4.

The results of the ANOVA test indicated significant differences among all groups for all

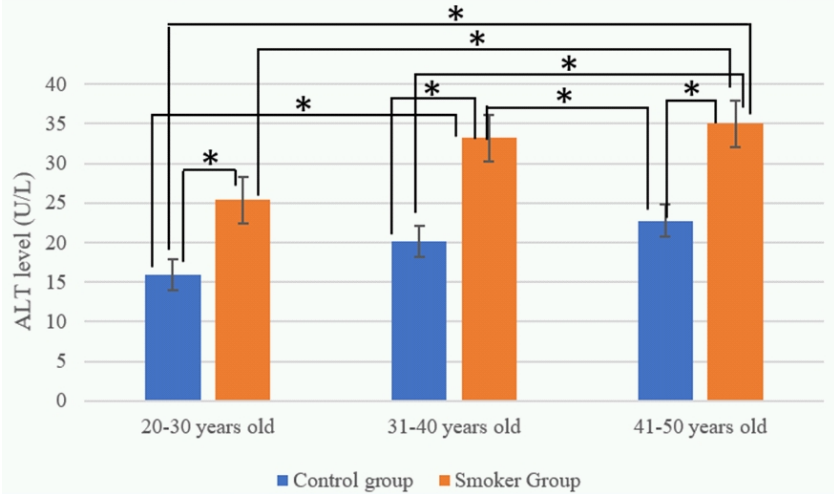

Figure 1. The ANOVA post-hoc analysis for ALT levels (U/L) among the groups (*) indicates a statistically significant difference with $p< 0.05$

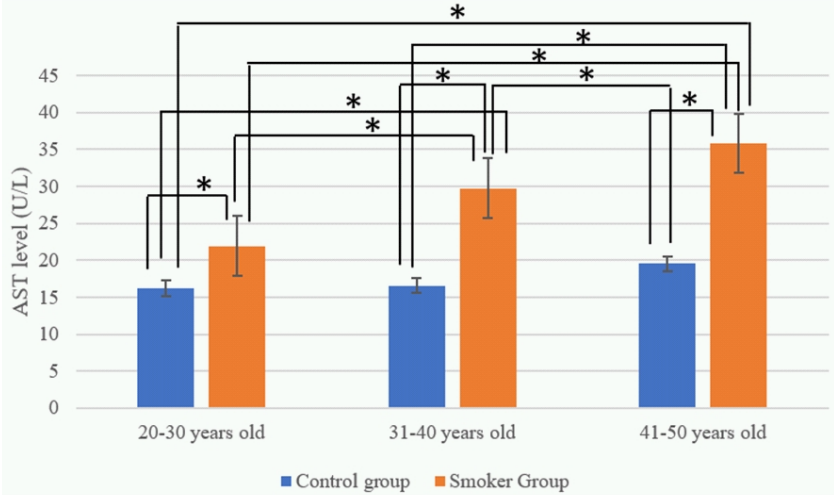

Figure 2. The ANOVA post-hoc analysis for AST levels (U/L) among the groups (*) indicates a statistically significant difference with $p< 0.05$

independent variables, namely ALT, AST, ALP, and CRP. To identify which specific group pairs exhibited the most significant differences, a follow-up post-hoc ANOVA test was conducted, as shown in Table 4. Significant differences in ALT values were observed between all control and smoker groups across all age categories. Similarly, AST values also showed significant differences between control and smoker groups in every age category.

Table 1 presents data indicating that the smoker groups had higher mean AST and ALT levels compared to the control groups. Although these mean values still fall within normal ranges, several smoker respondents exhibited elevated AST and ALT levels. This finding necessitates further testing and analysis of daily lifestyle habits to determine whether these elevated values may serve as early markers of future liver function impairment.

In addition to AST and ALT, ALP levels were also elevated in the smoker groups compared to controls. Post-hoc ANOVA analysis revealed that significant differences in ALP values varied by age. The most pronounced differences were observed between smokers aged 31–40 and 41–50 years and controls aged 31–40 years. The impact of smoking appears statistically significant beginning at age 31, while smokers aged 20–30 did not differ significantly from any other group, likely due to shorter smoking duration.

Smoking habits were also associated with inflammation, as indicated by the CRP parameter across various age groups in both cohorts. Plasma CRP concentrations increased notably in individuals aged 31

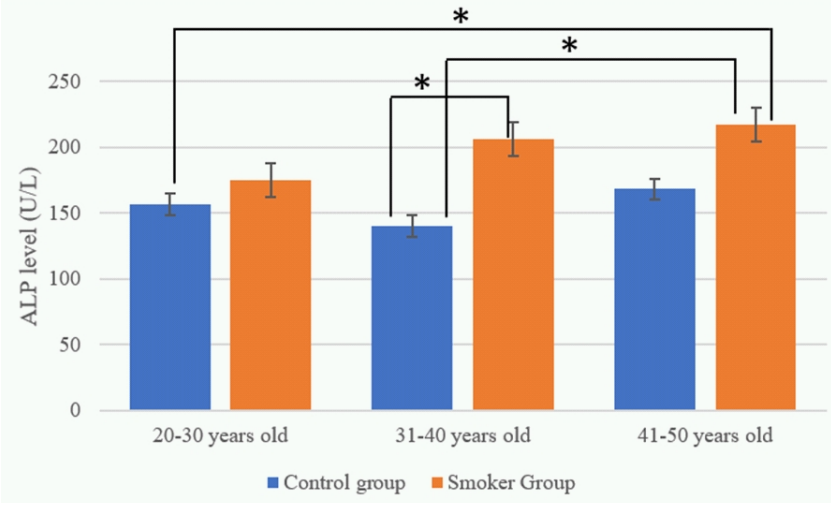

Figure 3. The ANOVA post-hoc analysis for ALP levels (U/L) among the groups (*) indicates a statistically significant difference with $p< 0.05$

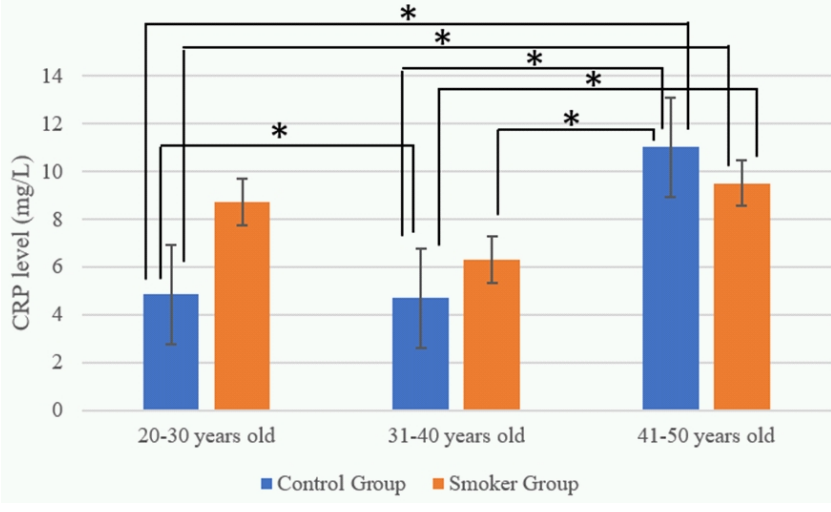

Figure 4. The ANOVA post-hoc analysis for CRP levels (mg/L) among the groups (*) indicates a statistically significant difference with $p< 0.05$

to 50 years and showed significant differences compared to other age categories in both groups. While inflammation can be triggered by multiple factors beyond smoking, smoking reduces immune defenses, making the body more susceptible to antigen or free radical exposure, which induces inflammation. The cumulative effect of long-term smoking and a high number of cigarettes smoked daily contributes to increased inflammation.

The parallel increase in AST, ALT, and ALP levels between ages 31 and 50 corresponds with elevated CRP levels in the same age range, serving as a warning signal for potential future liver function deterioration. The relationship between age ranges across groups and liver function and inflammation parameters was further analyzed using linear regression, the results of which are presented in Table 5.

Table 5 presents a summary of the linear regression results, indicating the strength of the correlation between age range and the concentrations of ALT, AST, ALP, and CRP, which are 0.652, 0.714, 0.397, and 0.259, respectively. These values demonstrate a positive correlation, as all coefficients approach 1, meaning that as age increases, the risk of liver function impairment also rises.

Additionally, Table 5 shows the coefficient of determination (r^2), which quantifies the proportion of variance in ALT, AST, ALP, and CRP values explained by age range. The strongest influence of age range was observed on ALT and AST levels, with coefficients of determination of 42.5% and 51%, respectively. This increase suggests that long-term smoking elevates the

TABLE 5
Correlation Between Age Range and Biomarkers of Liver Function and Inflammation

Parameter	Significance	Correlation value	Coefficient of determination (r square)	F count	T table
ALT	0.000	0.652	42.5%	74	0.6769
AST	0.000	0.714	51%	104	
ALP	0.000	0.397	15.8%	18.73	
CRP	0.009	0.259	6.7%	7.20	

risk of liver function damage, as indicated by rising ALT and AST levels with advancing age, particularly among smokers compared to controls (Table 1).

The relationship between age and ALP and CRP levels was less pronounced, with coefficients of determination of 15.8% and 6.7%, respectively. This implies that each increase in age corresponds to a modest increase in ALP and CRP values by these percentages.

Overall, the duration and frequency of smoking, as represented by the age range of smokers, show a strong correlation with increased ALT and AST values, indicating a gradual hepatocellular injury. ALT and AST are enzymes directly released into the bloodstream when hepatocyte damage or inflammation occurs. Conversely, ALP and CRP levels may remain normal or only slightly elevated because liver damage has not yet progressed to systemic inflammation or biliary obstruction.

Therefore, ALT and AST values can serve as important early biomarkers for monitoring potential liver function impairment in individuals who have smoked for prolonged periods.

DISCUSSION

This research analyzed the relationship between smoking and the decline in liver function as well as the occurrence of inflammation in the productive age group (20–50 years). The liver function parameters included ALT, AST, and ALP, along with the inflammatory marker CRP. The study compared these parameters and the incidence of inflammation between smoker and control groups, each subdivided by age categories of 20–30 years, 31–40 years, and 41–50 years.

Based on the results presented in Table 1, a trend of increasing liver function and inflammation parameters with advancing age was observed in both smokers and controls. The mean levels of ALT, AST, ALP, and CRP in the smoker group were consistently higher than those in the control group. Moreover, these parameters increased with age, as evidenced by the highest values observed in the 41–50 year age group. Thus, the data demonstrate an age-related increase in ALT, AST, ALP, and CRP levels, with significantly higher values in the smoking group. Although the majority of liver function values in the respondents remained within normal limits, the smoker subgroup aged 41–50 exceeded the normal range. Meanwhile, inflammatory parameters in both groups were elevated beyond normal thresholds. Comparative analyses between smoker and control groups using ANOVA and post hoc tests revealed significant differences in ALT and AST levels across all age categories, whereas ALP values did not significantly differ between groups. ALP levels in both groups remained within the normal range but tended to rise with age among smokers. For the inflammatory marker CRP, significant differences between smokers and controls emerged in the 31–40- and 41–50-year age groups.

The upward trend of liver function decline and inflammation in smokers with increasing age is suspected to be influenced by lifestyle habits within this group. As shown in Table 2, smokers frequently inhabit environments with other smokers. As age increases, the number of cigarettes smoked per day also rises (>20 cigarettes), along with longer smoking durations (>5 years). Most smokers began their habit during adolescence (ages 15–20). This indicates that increasing age, smoking environment, daily cigarette consumption, and smoking duration collectively contribute to the elevation of ALT, AST, ALP, and CRP levels. Hackshaw *et al*. demonstrated that even smoking a single cigarette per day carries health risks; light smokers (1–5 cigarettes daily) face up to a 65% increased risk of coronary heart disease and stroke, risks that escalate with greater cigarette consumption, especially among heavy smokers (20 cigarettes per day).[15] These findings support the higher liver function impairment and inflammation markers observed in smokers compared to controls. Smoking can disrupt liver function despite the liver not being in direct contact with smoke, as it serves as the organ responsible for the biotransformation of drugs, alcohol, and other harmful substances.[16]

Lifestyle factors also contribute to liver function decline and inflammation. Research by Nivukoski *et al*. revealed associations between unhealthy lifestyle

factors––such as alcohol consumption, smoking, overweight status, and insufficient physical activity––and abnormalities in laboratory tests for liver function, inflammation, and lipid profiles, including ALT, GGT, CRP, and lipid profiles.[17] Respondents' lifestyle habits were assessed via interviews and the Chronic Liver Disease Questionnaire (CLDQ) to clarify whether smoking or other lifestyle factors contributed to liver function decline and inflammation. The CLDQ was employed to evaluate the impact of chronic liver disease on respondents' quality of life.

Table 3 details lifestyle data in smokers and controls. Alcohol consumption (both frequent and occasional) was more prevalent among smokers, although most respondents in both groups reported no alcohol use. Consumption of small amounts of alcohol (1–4 times per day) is not associated with liver damage risk; however, heavy drinking increases the risk of liver damage such as cirrhosis. This is because the liver can regenerate and maintain function if alcohol intake is low, but excessive intake impairs liver function and leads to damage.[18]

Physical activity frequency of 1–3 times per month was more common in the control group than among smokers. More smokers aged 31–40 and 41–50 years reported no exercise, though routine physical activity (1–3 times per week) was more frequent in the 2030-year smoker group. This pattern likely influences liver function parameters, as lower ALT, AST, and ALP levels were observed in the younger smoker subgroup compared to older smokers. This aligns with findings from Hejazi and Hackett, who showed that exercise improves liver function in patients with non-alcoholic fatty liver disease (NAFLD), demonstrated by reductions in ALT and AST following aerobic and resistance training.[19]

Sleep duration in both groups was predominantly 5–7 hours per day, indicating suboptimal rest. Prior studies have associated short sleep duration (<5 hours) with NAFLD incidence, though 5–7 hours has not been linked to significant liver damage.[20] The study also examined body mass index (BMI) to liver function and inflammation parameters, finding a correlation between obesity and elevated ALT and AST levels.[21] More smokers were overweight compared to controls, although most respondents in both groups had normal BMI.

The findings confirm that smoking adversely impacts the liver, evidenced by elevated ALT, AST, and ALP levels in smokers. This corroborates research by Fathima and Kalyanikutty, who reported that smoking increases liver function parameters.[22] Cigarette smoke contains free radicals such as nicotine, tar, and carbon monoxide, which induce oxidative stress and reduce antioxidant defenses, causing elevated ALT and AST in the blood. Prolonged exposure to free radicals and tobacco constituents progressively increases hepatocyte damage risk.[23,24]

Prekumar *et al*. demonstrated a positive association between smoking and elevated ALP levels; however, ALP elevation may also reflect other conditions such as active growth, osteoporosis, and renal impairment, making it a sensitive but nonspecific marker.[25] Correspondingly, Table 1 shows the greatest increases in ALT, AST, and ALP in the 41–50-year age group. As cumulative cigarette consumption rises with age, risk factors for osteoporosis and kidney disease also increase.[26,27]

Regarding inflammation, Table 1 indicates significant CRP differences between smokers and controls only in the 31–40- and 41–50-year age groups. Both groups' CRP levels exceeded normal thresholds, reflecting CRP's nature as a sensitive but nonspecific marker that can rise due to infection, rheumatoid arthritis (RA), cardiovascular diseases, trauma, and progressive cancer.[28] Elevated CRP in the control group likely results from factors other than smoking or liver dysfunction.

Smoking impairs the liver through three mechanisms: toxic, immunologic, and oncogenic pathways.[29] The direct toxic effect involves oxidative stress induced by smoke components, leading to hepatic fibrosis. Smoking increases proinflammatory cytokines such as interleukin (IL)-1, IL-6, IL-8, and tumor necrosis factor α, resulting in liver injury. Indirect toxic effects include secondary polycythemia––elevated carboxyhemoglobin due to reduced oxygen-carrying capacity––stimulating erythropoietin production and red blood cell count. Increased hemolysis releases iron, which accumulates in hepatocytes via macrophage uptake, promoting oxidative stress and liver damage.

Immunologically, nicotine suppresses lymphocyte proliferation and differentiation, decreases antibody production, induces lymphocyte apoptosis, increases cytotoxic CD8+ T cells, decreases CD4+ T cells, and impairs natural killer (NK) cell activity. Oncogenic effects stem from carcinogens in cigarettes, such as hydrocarbons, nitrosamines, tar, and vinyl chloride. The compound 4-aminobiphenyl in tobacco elevates hepatocellular carcinoma risk. Smoking also downregulates tumor suppressor genes like p53, facilitating neoplasm development.[29,30] Active smoking is linked to non-alcoholic fatty liver disease (NAFLD), fibrosis, and hepatocellular carcinoma.[31]

In this study, ALT and AST levels in both groups remained within normal ranges except for smokers aged 41–50, whose values exceeded normal limits. ALP levels in both groups stayed within normal ranges. This suggests that liver damage in smokers aged 41–50 likely affecting hepatocytes but not bile ducts. ALT and AST are markers of hepatocyte damage and cell death, while ALP elevation indicates bile duct injury or obstruction.[32] Elevated CRP levels beyond normal in both groups imply

ongoing inflammation potentially triggered by infections, autoimmune disease, obesity, or lifestyle factors such as insufficient sleep, stress, poor diet, and medication use.[33] CLDQ questionnaire results (Table 3) showed no significant differences between groups, indicating that chronic liver disease symptoms were not clinically apparent in either group.

The combination of aging, smoking habits, and unhealthy lifestyle factors contributes to increased liver function impairment and inflammation parameters. Significant elevations in ALT, AST, ALP, and CRP were first observed in the 31–40 age group compared to controls. Respondents aged 31–40 and 41–50 had longer smoking durations (>5 years) and earlier smoking initiation (under 15 years). These groups also reported reduced physical activity and more overweight prevalence. Therefore, the rise in ALT, AST, ALP, and CRP in smokers relative to controls likely reflects smoking, age, and lifestyle factors. Healthy behaviors such as not drinking alcohol, regular exercise, sufficient sleep, and normal body weight may help maintain liver function and inflammatory parameters within normal ranges. This is further supported by CLDQ data showing no deterioration in quality of life from liver disease among respondents.

CONCLUSION

This study demonstrates a significant association between smoking and impaired liver function, as well as increased systemic inflammation, particularly in individuals aged 31–50 years. Smokers exhibited higher levels of ALT, AST, ALP, and CRP compared to non-smokers, with significant elevations emerging from the 31–40 age group onward. These findings suggest a cumulative effect of smoking over time, further influenced by lifestyle factors such as alcohol use, physical inactivity, and higher BMI.

Despite enzyme levels remaining mostly within normal ranges, elevated values in older smokers indicate potential subclinical hepatic injury. Smoking appears to contribute to liver dysfunction via oxidative stress, immune modulation, and inflammatory pathways. While CLDQ scores showed no significant impact on perceived quality of life, the biochemical changes highlight the importance of early intervention. Promoting healthy lifestyles and smoking cessation may help to prevent progressive liver damage and systemic inflammation

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