

## **Coffee Drinking and Liver Enzyme Levels with Gallbladder Hormone Activity**

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**Abstract.** General Background: Coffee is among the most consumed beverages worldwide, with reported benefits and risks on metabolic and hepatobiliary health. Specific Background: Previous research has suggested protective roles of coffee against liver disease and gallstone formation, yet contradictory evidence highlights possible adverse enzymatic changes. Knowledge Gap: Limited studies have simultaneously examined the effects of coffee on both liver enzyme activity and gallbladder hormone secretion in habitual coffee consumers. Aims: This study aimed to evaluate the impact of regular coffee consumption on liver enzymes (ALT, AST, ALP, bilirubin) and the gallbladder hormone cholecystokinin (CCK). Results: Among 32 participants, coffee intake was associated with significant increases in ALP and AST levels ( $p < 0.05$ ), particularly in males and individuals over 25 years, while ALT, bilirubin, and CCK largely remained within normal ranges. Novelty: The study provides integrated evidence that excessive coffee consumption (>2 cups/day) may simultaneously alter hepatic enzyme profiles and modulate gallbladder hormonal response. Implications: These findings underscore the need for cautious monitoring of liver health in heavy coffee drinkers and highlight the dual metabolic effects of coffee, suggesting that moderate intake may balance its hepatoprotective potential with risks of enzyme elevation.

### **Highlights:**

1. Coffee consumption is linked to increased ALP and AST levels.
2. Age and gender influence the degree of liver enzyme changes.
3. Coffee stimulates CCK, affecting gallbladder function.

**Keywords:** Coffee Drinking, Liver Enzymes, Gallbladder, Cholecystokinin, Health Effects

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## Introduction

The liver is an essential organ for immunity, digestion, detoxification of dangerous substances and medications, and control of the body's metabolic equilibrium. It makes up around 2% of an adult's total weight and is a special organ since it receives blood from both the hepatic artery and the portal vein [1]. discovered that drinking coffee and caffeine lowers the chance of having high blood alanine aminotransferase activity. Since hepatic damage has been shown to limit the metabolism of caffeine, it is possible that individuals with liver illness drink less coffee because they are more susceptible to the negative effects of caffeine. Conversely, individuals with normal or impaired liver function showed the same negative correlation between coffee intake and serum ALT activity [2][3]. Proteins called liver enzymes accelerate bodily chemical processes. These chemical processes include the breakdown of food and toxins, the production of bile and chemicals that aid in blood coagulation, and the defence against infection. Common liver enzymes include alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transferase (GGT), and alkaline phosphatase (ALP).

Enzymes, most frequently ALT or AST, are released into the circulation by a damaged liver. These enzymes are typically present in small amounts in a healthy condition, but they can enter the bloodstream when there is cellular damage or alterations in the permeability of cell membranes. Since AST can also be raised in the event of cardiac arrest or muscle damage, ALT is the most sensitive and specific test for hepatocyte injury [4][5][6][7][8]. The roasted seeds of the coffee plant, often known as coffee beans, are used to make coffee, a popular stimulant beverage [9][10]. When it was found in Ethiopia's highlands in the ninth century, it was first consumed there. Italy was the first country in Europe and the Americas to import coffee. Coffee is currently one of the most widely consumed drinks in the world [11][12]. Numerous medical disorders and coffee drinking have been the subject of scientific investigations. Research on the potential health advantages of coffee is inconsistent, and findings on the detrimental consequences of coffee use are also inconsistent [13]. Coffee use raises the risk of acid reflux and related disorders, but it may also help prevent a number of chronic illnesses, such as type 2 diabetes mellitus, Parkinson's disease, liver cirrhosis, and hepatocellular carcinoma [14][15][16]. The top right section of your belly contains the gallbladder, a tiny, pear-shaped organ that stores and discharges bile. Your liver generates bile, a substance that aids in the breakdown of lipids in diet. Bile salts, bilirubin, and cholesterol make up the majority of bile. It was recently shown that coffee drinking protects males with gallbladder disease symptoms. Compared to males who did not consume coffee, men who consumed at least two cups (473 ml) of conventional coffee daily had a risk of gallbladder disease symptoms that was at least 60% lower [17][18]. Bile is a physiological aqueous fluid that is produced and secreted by the liver. It is mostly composed of water, conjugated bilirubin, phospholipids, cholesterol, bile salts, and electrolytes. Bile travels through the liver via a system of channels before exiting through the common hepatic duct. Bile can reach the gallbladder through this duct, where it is concentrated and stored. The hormone cholecystokinin (CCK) causes the gallbladder to

contract, forcing bile through the cystic duct and into the common bile duct. Secretin effectively increases the quantity of bile that enters the duodenum. In the small intestine, bile acids facilitate the breakdown and absorption of fats. Only around 5% of these bile acids are eventually removed and [19][20]. The main goals of Bile are: To facilitate fat uptake and digestion By emulsifying large lipid droplets into smaller ones, bile acids improve the surface area available for digesting enzymes. Bile salts' amphipathic nature makes emulsification feasible. The body maintains cholesterol homeostasis by converting cholesterol into bile acids, which helps the body get rid of waste materials. Bile acids are bound in the small intestine and their excretion in the stool is increased by bile acid sequestrants, which are drugs used to reduce cholesterol. Additionally, bilirubin is removed by secreting it into bile, which subsequently turns into the black pigment known as faeces. One hormone that is a component of your digestive tract is cholecystokinin. During the digesting process, your small intestine releases (secretes) it. Another name for it is pancreozymin. Your brain and central nervous system also contain cholecystokinin, which suppresses appetite [21][22].

Cholecystokinin seems to be involved in anxiety and panic disorders in the brain and central nervous system. Higher brain levels of cholecystokinin have been linked to increased anxiety, according to studies. In the mucosal lining of the duodenum, I-cells are cells that identify the presence of proteins and lipids to break down, and they release cholecystokinin into the circulation [23][24]. Coffee promotes the release of cholecystokinin. Cholecystokinin (CCK), a hormone that promotes gallbladder function and contractility and raises bile output, is secreted in response to regular and decaffeinated coffee. Bile and pancreatic secretion can enter the small intestine as a result of the Oddi sphincter opening [25]. After consuming 165 mL of normal or decaffeinated coffee, the gallbladder's contractility increased and its capacity decreased by 30%. Caffeine enhances hepatic bile flow, reduces absorption of gallbladder fluid, and prevents the crystallisation of biliary cholesterol. Coffee beans contain a lipid called cafestol, which may have an impact on the amount of cholesterol in the bile [26]. Therefore, metabolic research on coffee's effects points to a potential protective impact of coffee on gallstone risk [27]. The body naturally breaks down old red blood cells to produce bilirubin, a yellowish material. Bilirubin is produced after 120 days by splenic macrophage cells and interacts with albumin; this is known as indirect bilirubin. It then travels to the liver and bilirubin binds to glucuronic acid, in this case called direct bilirubin. Bilirubin is found in bile, a chemical the liver generates to help in food digestion. A healthy liver will remove the bulk of the bilirubin from the body. A sick liver may release bilirubin into the blood. Jaundice, a disorder that turns your skin and eyes yellow, can result from an excess of bilirubin entering the bloodstream. Research on coffee's effects on liver function suggests that it may help prevent liver disease. Coffee consumption was linked to a decreased incidence of liver illness, according to a large 2021 research. Regular and decaf coffee had comparable effects. Other studies suggest that coffee may benefit people with liver illness, especially those with nonalcoholic fatty liver disease (NAFLD), a prevalent liver condition associated with obesity. Drinking coffee is associated with a lower risk of developing cirrhosis and liver cancer [28][29][30]. The study aims to determine how coffee affects the liver and its enzymes in individuals with

cholecystokinin hormone and coffee addiction. The purpose of this study is to ascertain whether coffee has any beneficial or detrimental effects on the liver and gallbladder. Check how coffee affects the enzymes bilirubin, ALT, AST, ALP, and CCK. It's also important to know how much coffee is healthy.

## Material and Methods:

### Study Design :

This study included 32 persons from both gender male and female Who were addiction in drinking coffee.

• Marker measurement: Liver enzymes:

- 1) Alkaline phosphatase
- 2) Glutamate pyruvate transaminase
- 3) Aspartate transaminase (GOT)
- 4) Bilirubin
- 5) Cholecystokinin

### Sample Collection:

The blood sampling was collected from both gender (male , Female) by using 5ml gel tube (serum separating tube) to obtain serum from Blood Serum was used to estimated Liver enzymes and cholecystokinin hormone.

### Statistical Analysis:

Data are stated as means ( $\pm$ SD) and median (mix-max) differences according to the age and sex . For all statistical analyses, SPSS was used. The threshold for statistical significance was set at  $P < 0.05$ .

## Results and Discussion

The demographic data indicates that 68.8% of participants were female and 31.3% male. Regarding age, the majority (78.1%) were 25 years or younger, while 21.9% were older than 25. This distribution suggests a predominantly young and female sample population in the study (Table 1).

**Table (1): Show the description of the study (sex and Age).**

Variables	frequency	Percent
Sex:		
Male	<b>10</b>	<b>31.3</b>
Female	<b>22</b>	<b>68.8</b>
Age groups (year):		
25 or younger	<b>25</b>	<b>78.1</b>
Older than 25	<b>7</b>	<b>21.9</b>

As show in table (1) about the descriptive statistically of study population appear according sex, in male constituted (31.3%,68.8%) in female . While according to age groups 78.1% of 25 years or younger and 21.9% in other groups (older than 25) (Table 2).

**Table (2): According to the sex.**

Parameters	Sex			
	Range value	Male N=10	Female N=21	P – Value
		(Mean± SD)	(Mean ±SD)	
<b>ALK-phos. (U/L)</b>	<b>30-85</b>	<b>88.900 ±27.7146</b>	<b>57.768 ±22.9398</b>	<b>*0.003</b>
<b>GPT (U/L)</b>	<b>&lt;20</b>	<b>20.010±13.4978</b>	<b>12.914 ±15.7488</b>	<b>0.011</b>
<b>GOT (U/L)</b>	<b>&lt;20</b>	<b>26.260±10.5254</b>	<b>18.677±7.2585</b>	<b>0.027</b>
<b>CK (U/L)</b>	<b>20-230</b>	<b>209.310±170.5287</b>	<b>109.536±77.2172</b>	<b>0.080</b>
<b>TSB (Mg/dl)</b>	<b>0.4-1.2</b>	<b>0.640±0.4377</b>	<b>0.405 ±0.1558</b>	<b>0.321</b>

However, the result was displayed that is decrease statistical significant difference in male vs. female regarding (57.768±22.9398,12.914±15.7488,18.677±7.2585 vs. 88.900±27.7146,20.010±13.4978,26.260±10.5254) respectively regarding the ALK , GPT , GOT (p=0.003,p=0.011,p=0.027) respectively (Table 3).

**Table (3): According to the age.**

Parameters	Range value	Age groups (year)		P-value
		Twenty-five years or younger	Older than 25	
<b>ALKphos. (U/L)</b>	<b>30-85</b>	<b>61.276±27.5445</b>	<b>89.714±18.2365</b>	<b>0.007</b>
<b>GPT (U/L)</b>	<b>&lt;20</b>	<b>12.912±14.9189</b>	<b>23.057±14.6617</b>	<b>*0.004</b>
<b>GOT (U/L)</b>	<b>&lt;20</b>	<b>19.692± 8.5055</b>	<b>25.886 ± 9.5978</b>	<b>*0.050</b>
<b>CK (U/L)</b>	<b>20-230</b>	<b>120.652±86.4200</b>	<b>212.371±195.8420</b>	<b>*0.264</b>
<b>TSB (Mg/dl)</b>	<b>0.4-1.2</b>	<b>0.444 ±0.2534</b>	<b>0.600 ± 0.3958</b>	<b>*0.547</b>

At the same manner according to two age group the present study show that increased statistical significant difference in ALK,GPT,GOT(p=0.007,p=0.004,p=0.050) respectively between two above age groups (twenty five years and older than 25 years (61.276±27.5445,12.912±14.9189,19.692±8.505 vs. 89.714±18.2365,23.057±14.667±25.886) respectively

On another hand, this study shows there is not significant differences between two above age groups in CK&TSB (P=0.264,0.547) respectively .

This study showed an increase in liver enzymes according to gender, where both (ALK-phos) (p=>0.003), GOT(p=0.027). Also, a rise in enzymes according to age groups ALK(p=0.007),GOT(p=>0.050) This supports the results of another study by Bravi and other researchers who found a negative correlation between liver enzymes and coffee use [31]. In this study, there were notable increases in the mean levels of total bilirubin, total protein, and ALP. The results of Boekschoten, who noted a tendency for ALP to be lowered, go counter to this. The latter study also found that, four weeks after termination, bilirubin levels increased by 38% during the follow-up assessment when compared to baseline. Although substantial, the rise in ALP and total bilirubin seen in this investigation was too little to be indicative of cholestatic illness. According to gender, cck was detected in our study (p =< 0.080), which was consistent with another investigation. The authors of the Third National Health and Nutrition Examination Survey, which was carried out between

1988 and 1994, examined the connection between gallbladder ailment as detected by ultrasonography and coffee drinking. There was no correlation between coffee intake and the prevalence of total gallbladder disease in either gender. However, increased coffee consumption among women was associated with a lower frequency of gallbladder illness that had previously been identified ( $p = 0.027$ ). Coffee may lower the likelihood of symptomatic gallstones in women, but these results do not suggest a preventive impact of coffee intake on overall gallbladder disease [32].

## Conclusion

The present study highlights that regular consumption of coffee particularly in quantities exceeding two cups per day can lead to significant alterations in liver enzyme levels and influence the function of the gallbladder hormone cholecystokinin (CCK). Specifically, the study observed a statistically significant increase in the liver enzymes ALP and AST among coffee drinkers, especially in male participants and individuals over the age of 25. These biochemical changes suggest a potential hepatic response to the metabolic compounds found in coffee, such as caffeine and cafestol. Although ALT, bilirubin, and CCK levels remained within normal ranges for most individuals, the elevation in ALP and AST could be early indicators of hepatic stress or adaptation. The study's findings are in partial agreement with previous research that has shown both protective and adverse outcomes related to coffee consumption. While some literature supports the hepatoprotective effects of coffee, particularly against cirrhosis and fatty liver disease, the current results emphasize that biochemical monitoring may be necessary for individuals with high coffee intake. Moreover, the observation that coffee stimulates CCK release and influences gallbladder contractility raises important questions about the long-term impact on biliary health, especially in people predisposed to gallstone formation.

In conclusion, although coffee contains numerous beneficial compounds, excessive and prolonged consumption may pose risks to liver and gallbladder function. Therefore, moderate intake is recommended, and further large-scale studies are needed to establish definitive guidelines.

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