

IMPACT OF COFFEE INTAKE ON LIVER RELATED DISEASES: A REVIEW

ARUN KUMAR, VIPIN GUPTA AND M. P. SACHDEVA

ABSTRACT

Coffee is currently the second highest consumed beverage in the world after water; its compounds possess antioxidants, anti-inflammatory, antifibrotic and anticarcinogenic properties. Epidemiological and clinical investigations have suggested that coffee consumption could reduce the risk of alcoholic liver cirrhosis, type 2 diabetes, non-alcoholic fatty liver disease, hepatocellular carcinoma (HCC), progression of non-alcoholic steatohepatitis (NASH), severity of fibrosis, as well as the activity of alanine transaminase (ALT) in liver injury patients. Studies suggest that two extra cups of coffee per day leads to reduced risk of liver related disease. So an attempt is made in this review, to highlight the current information related to inverse association between coffee intake and liver related diseases.

Key words: Coffee, Liver disease, Obesity, Liver Enzymes

INTRODUCTION

Many years ago Ponte *et al.* (2002) pointed out that coffee was the world's second highest consumed beverage after water, with approximately 500 billion cups drunk every year. It contains compounds like; caffeine, chlorogenic acid and diterpenes which possess antioxidant, anti-inflammatory, anti-fibrotic and anticarcinogenic properties (Spiller *et al.* 1984). Liver related diseases like non-alcoholic fatty liver disease (NAFLD) are on increase and affect both adults and children (Yu *et al.* 2002). Epidemiological and clinical investigations have suggested that its consumption could reduce the risk of alcoholic liver cirrhosis, type 2 diabetes (Dickson *et al.* 2015), NAFLD (Graeter *et al.* 2015), hepatocellular carcinoma, the progression of non-alcoholic steatohepatitis (NASH) (Molloy *et al.* 2012), as well as the activity of ALT (alanine transaminase) in liver injury patients (Dickson *et al.* 2015). In this review an attempt is made to highlight the current information related to inverse association between coffee intake and liver related diseases.

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COFFEE AND NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Studies conducted in various regions of the world have shown inverse association between coffee and liver related disease especially with NAFLD. For intense; Birerdinc *et al.* (2012) conducted a study using National Health and Nutrition Examination Surveys (NHANES 2001–2008) data, and found that caffeine intake was independently associated with a lower risk for NAFLD [OR = 0.999319, 95% CI (0.998955–0.999684) $p = 0.0003$]. A cross-sectional study from non-alcoholic Steatohepatitis Clinic Research Network (NASH CRN) from 2004 to 2008 reported that coffee intake was inversely associated with advanced fibrosis among NAFLD patients ($n = 782$) with lower HOMA-IR (i.e. a lower odds of advanced fibrosis (OR=0.64; 95% CI, [0.46–0.88], $p=0.001$)) (Bambha *et al.* 2014). Another study based on the medical records of the Brooke Army Medical Center Hepatology Clinic (Fort Sam Houston, TX) suggested that coffee consumption was associated with a significant reduction in risk of fibrosis among NASH patients (Molloy *et al.* 2012).

Further, a recent study observed that high coffee intake was significantly associated with reduced risk of advanced liver fibrosis even in HIV-HCV co-infected patients from ANRS CO13 HEPAVIH cohort ($n = 1019$) with high-risk alcohol consumption (Yaya *et al.* 2018). The protective effects of coffee drinking against NAFLD have also been reported using case control design (Gutierrez *et al.* 2012); an association with less severe bright liver score (BLS) as compared with obesity, higher insulin resistance, lower HDL cholesterol, older age and arterial hypertension are associated with a greater risk of more severe BLS (Catalano *et al.* 2010). Another recent study from TE liver clinic Monash Medical Centre (Melbourne Australia, $n = 1018$) found that consuming 2 or more cups of coffee per day had a lower liver stiffness ($p = 0.044$), after adjustment with age, gender, smoking, alcohol consumption and disease state (NAFLD, HCV, and HBV status) (Hodge *et al.* 2017).

COFFEE WITH LIVER ENZYMES AND LIVER STIFFNESS

The level of liver enzymes has been most commonly used method for assessing the injury in liver cells (Whitfield, 2001). Several studies from European and Japanese populations have suggested an inverse association between coffee and levels of g-glutamyltransferase and aminotransferases in serum (Arnesen *et al.* 1986; Casiglia *et al.* 1993; Pintus 1996; Nakanishi *et al.* 2000). A study on intake of caffeinated and decaffeinated coffee revealed that caffeinated coffee has significant inverse associations with ALT ($\hat{a} = -0.08$, $p = 0.0111$), and AST ($\hat{a} = -0.05$, $p = 0.0155$). In contrast, decaffeinated coffee showed no significant associations with liver enzymes (Dickson *et al.* 2015).

Coffee consumption has also been shown to be protective in liver stiffness. Rotterdam study (ongoing prospective population-based cohort $n = 2,424$) suggested that proportion of liver stiff measurement (LSM) (~ 8.0 kPa) decreased with higher coffee consumption (7.8%, 6.9% and 4.1% for no, moderate and

frequent, respectively; $P_{\text{trend}} = 0.006$). Data revealed an inverse association after using multivariable regression ($OR_{\text{mod}} 0.75$, 95% CI 0.33-1.67; $OR_{\text{freq}} 0.39$, 95% CI 0.18-0.86; $p = 0.005$) after adjusted with other lifestyle and environmental factors (Alferink *et al.* 2017).

COFFEE AND HEPATOCELLULAR CARCINOMA

Coffee intake not only showed inverse association with early stages of liver disease like NAFLD, NASH but evidence of its association with advanced stages like HCC was also found; a meta-analysis on association of coffee intake with HCC suggested that two extra cups of coffee per day is associated with a 35% reduction in the risk of HCC (RR 0.65, 95% CI 0.59 to 0.72) (Kennedy *et al.* 2017). A large cohort association study among 60,323 Finnish participants (25-74 years and free of any cancer at baseline) shown an inverse and graded association of coffee with the risk of liver cancer (Hu *et al.* 2008). Further, a meta-analysis of twenty cohort studies has suggested that there is a significant inverse linear dose-response association between coffee consumption and liver cancer risk ($p = 0.36$) (Yu *et al.* 2016).

No Protective Effect of Coffee with Liver Related Disease

However, there are studies that have found no protective association of coffee intake on liver related disease like; no protective effect of coffee consumption on fatty liver, serum ALT concentrations ($n=1223$ from Echinococcus multilocularis and other internal medical disorders in Leutkirch (EMIL)) (Graeter *et al.* 2015) and advanced fibrosis among individuals with higher HOMA-IR ($p=0.6$) (from Adults of NASH CRN) (Bambha *et al.* 2014). A recent study has also found no association of coffee intake with any lower odds of hepatic steatosis with non-alcoholic ($n = 916$) ($OR = 0.93$; 95% CI: 0.72-1.20 $p = 0.28$) or with alcoholic forms ($n = 276$) ($OR = 1.20$; 95% CI: 0.66-2.0 $p = 0.57$) from Mediterranean area after adjusting the confounders (Veronese *et al.* 2018).

CONCLUSIONS

We may look to coffee as one arrow in the quiver of therapies and lifestyle approaches to tackle the problem of liver diseases, and the moderate coffee consumption may be a benign adjunct to the comprehensive management of patients with liver disease. Longitudinal studies are needed to further investigate the impact of coffee consumption on liver related diseases.

Conflicts of interest: No conflict to declare.

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