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Original Research Article

Effect of coffee in prevention of non-alcoholic fatty liver disease

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ABSTRACT

Background: Non-alcoholic fatty liver disease which is also known as metabolic associated fatty liver disease is characterized by accumulation of fat in liver without any underlying clear etiology such as chronic alcohol abuse. Our study aimed to evaluate the effect of coffee in prevention of non-alcoholic fatty liver disease and its effect on various biochemicals like lipids, ESR, CRP, ferritin etc.
Methods: We conducted a retrospective study in a tertiary care public sector hospital. The study was conducted among 300 patients. 150 had confirmed diagnosis of NAFLD through ultrasound abdomen and 150 had normal liver on ultrasound abdomen. Both study groups were asked to fill a predetermined questionnaire which included questions on amount of coffee and other caffeinated beverages, physical activity, and demographic data. P value of less than 0.05 was considered significant.
Results: Study compared the effect of coffee on prevention of non-alcoholic fatty liver disease (NAFLD). We found that subjects who did not drink coffee had more odds of developing NAFLD as compared to those who did. Inflammatory markers and lipid profile were found to be lower in those who drank coffee as compared to those who did not.
Conclusions: Based on multiple studies done on mice and rat at molecular level and our study, we conclude that various components present in coffee play a significant role in preventing NAFLD, liver fibrosis and even liver cancer. Coffee has also shown to have anti-inflammatory properties and lowers lipid level in blood.

Keywords: Coffee, Fatty liver, Liver fibrosis, NAFLD

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) which is also known as metabolic associated fatty liver disease is characterized by accumulation of fat in liver without any underlying clear etiology such chronic alcohol abuse.[1] NAFLD is divided into two subtypes, non-alcoholic steatohepatitis (NASH) and nonalcoholic fatty liver (NAFL).[2] NAFLD eventually progresses to NASH and later progresses to liver failure, liver cancer, or cirrhosis. The most common risk factor for NAFLD are diabetes mellitus, obesity, metabolic syndrome X, and age.[3] Some studies have reported prevalence of NAFLD in overweight patients to be above 70% and over 90% in morbidly obese patients.[4] Prevalence of NAFLD has been reported to be significantly more in Hispanic population and least in non-Hispanic Blacks.[5]

NAFLD is the most common form of liver disease in the world with prevalence of 24% worldwide.[6] NAFLD has been more commonly seen in developed countries, which is mainly attributed to lifestyle choices. Management of NAFLD includes lifestyle modification with weight loss and dietary changes. There is some evidence that supports the use of Vitamin E and thiazolidinedione primarily pioglitazone in NAFLD; however more studies are needed to confirm its clinical benefit.[7] The most common cause of chronic liver disease is NAFLD. Preventing the

development of NAFLD is important as in United States alone, it is estimated that 35% of adults have NAFLD with 10% adults having NASH. It is estimated that the financial burden of NAFLD in United States is over a 100 billion dollar per annum.[8] Few studies have established an association between coffee consumption and development of NAFLD. Studies have attributed the beneficial effect of coffee through variety of mechanisms including prevention of liver fibrosis, gene modulation, and molecular signaling.[9-16]

The purpose of our study was to evaluate the association between coffee consumption and its effect of prevention of NAFLD.

METHODS

We conducted a retrospective study in a tertiary care public sector hospital. Data was collected for a period of 5 months from May 2020 to September 2020. The tertiary care hospital provides medical care for approximately 800000 patients per year. The study was conducted among 300 patients. 150 had confirmed diagnosis of NAFLD through ultrasound abdomen and 150 had normal liver on ultrasound abdomen. Both study groups were asked to fill a predetermined questionnaire which included questions on amount of coffee and other caffeinated beverages, physical activity, and demographic data. The amount of caffeine intake was further divided into 1-2 cups (150 ml), 3-4 cups and >4 cups of coffee per week.

Inclusion criteria

All patients above the age of 18 years were included in the study.

Exclusion criteria

Patients who had history of current or previous alcohol use, history of hepatitis infection or drug induced hepatitis were not included in both groups.

Study population in both groups was included only after carefully adjusting for variation in age, gender and BMI of the participants such that the average age, gender and BMI of the study population were approximately same. Not taking caffeine was consider as having an exposure or risk factor and taking caffeine was considered as not having a risk factor or exposure. After collection of the data from the questionnaire, the odds of developing NAFLD in those who were not taking caffeine (exposure present) as compared to those who were taking caffeine (exposure absent) was determined. Other laboratory testing like liver function test, glucose, lipid profile and inflammatory marker like ESR, CRP and ferritin was also included in the study.

Microsoft 2010 excel sheet was used for data analysis. P value of less than 0.05 was considered significant. The study protocol was approved by the Institutional Review Board and all participants provided written informed consent.

RESULTS

The study was performed for 5 months during which data was collected from laboratory, imaging studies and questionnaire as provided by 300 patients. 150 (50 percent) patients had confirmed diagnosis of non-alcoholic fatty liver disease on ultrasound and 150 (50 percent) patients had normal liver findings on ultrasound. There were 92 (61 percent) males and 58 (39 percent) females in control group and 95 (63 percent males) and 55 (37 percent) females in case group. Median age of the study population in case group was 49 (18-65) years and 46 (18-64) years in control group. Median body mass index was 25.6 (21-28) in case group and 25 (21-29) in control group.

In the case group 57 (38 percent) of the patients had regular caffeine intake. With 6 (4 percent) having 1-2 cups per week, 15 (10 percent) having 3 to 4 cups per week and 36 (24 percent) having more than 5 cups of coffee per week. In the control group, 92 (61 percent) of the patients had regular caffeine intake, with 17 (11 percent) having 1 to 2 cups per week, 35 (23 percent) having 3 to 4 cups per week and 40 (27 percent) having more than 5 cups of coffee per week.

Table 1: Prevalence of disease on the basis of caffeine exposure.

Exposure	Disease	
	Present	**Absent**
Present	93	58
Absent	57	92
Total	150	150

Overall, there was significantly more subjects who developed NAFLD in group that were not taking caffeine OR 2.5 (95% CI 1.2-3.5), p<0.03). On comparing the group that drank 1-2 cups of coffee per week; there was no statistical significance in development of NAFLD in either group OR 2.3 (95% CI 0.8-3.1), p<0.04). In the group that drank 3-4 cups of coffee per week and those who drank >4 cups of coffee per week were found to have statistically significant decrease in NAFLD in subjects who drank coffee as compared to those who did not, OR 2.4 (95% CI 1.5-2.8), p<0.02) and OR 1.9 (95% CI 1.1-2.6), p<0.02) respectively. In the subjects who had high coffee consumption, there was also increased consumption of sugar, decreased physical activity and hyperlipidemia. BMI, age and gender of both groups with high coffee consumption were found to be approximately the same. There was found to be decreased prevalence of hyperlipidemia in subjects who had more caffeine consumption, but the statistical significance could not be determined because of low sample size. Average blood glucose in subjects with high coffee consumption was

also found to be higher as compared to subject who did have regular caffeine consumption. Inflammatory marker like CRP, ESR and ferritin were found to be lower in subjects who had caffeine consumption as compared to the other group. There was no difference observed between groups in there liver enzyme levels.

DISCUSSION

Our study aimed at evaluating the association between coffee consumption and its effect on prevention of non-alcoholic fatty liver disease. We also aimed at evaluating the role of coffee in altering the various biochemical levels in the blood like inflammatory markers, lipids, glucose and liver enzyme. In our study we found positive association between coffee consumption and development of NAFLD. There are very few retrospective or prospective studies done to evaluate this association. Most of the studies have been done on mice and rats. Most studies have demonstrated that coffee has a protective role on liver through various biochemicals present in coffee like chlorogenic acid (CGA), trigonelline, diterpenes kahweol, cafestol, 16-O-methylcafestol, melanoidins and caffeine. Ma et al in their study on mice showed the chlorogenic acid (CGA) improves liver steatosis, insulin sensitivity and reduces chronic inflammation.[9] Wang et al in there in vitro cell study established that caffeine inhibited the production of procollagen I via PKA-SRCERK1/2 and procollagen III via P38 MAPK 0 pathway and hence prevents liver fibrosis.[10] Another in vitro study established that trigonelline suppresses reactive-oxygen-species (ROS)-potentiated invasive activity and thereby progressing of liver fibrosis.[11] A review study mentions role of diterpenes kahweol, cafestol and 16-O-methylcafestol, in prevention of NAFLD by inducing phase II detoxifying enzymes, and regulation of Nrf_2/ARE signalling pathways, and hence enhances the endogenous defence systems against oxidative damage.[12]

In our study we found that coffee has an anti-inflammatory role which is in agreement with many studies done on mice and rats. Paur et al in their study on mice showed that melanoidins, reduces inflammation by a 63% inhibition of nuclear factor-jB activation which has been associated with the progression of liver fibrosis.[13] Vitaglione et al in a study on rats showed that coffee/polyphenol modulates gene and protein expression of several mediators of inflammation, insulin sensitizers, and hepatic fat b-oxidation by up-regulation of PPAR-alpha and adipo R_2, and down regulation of THF alpha, TGF beta and tTG gene which decreases the progression to NASH. Also reduces IFN gamma and reduces GST activity and increase the concentration of IL_4, IL_{10} and GSH/GSSG which also play a role in decreasing the progression to NASH. Few other studies also came to a similar conclusion.[14-16] Chlorogenic acid and caffeic acid have also been found to have anti- exhibit protective effects against ischemia reperfusion injury through its antioxidant properties.[17]

In our study we found that the subjects who were drinking coffee had lower lipid levels as compared to those who were not. Statistical significance could not be determined because of low sample size but this finding is in agreement with many studies that attributed role of chlorogenic acid and caffeine in reduction of hepatic TG levels.[18-21] This role of coffee in decreasing lipid level has been shown to have a protective role in prevention of NAFLD by Ray et al in their in vitro study which demonstrated that caffeine induces autophagosome formation in $HepG_2$ cells which reduced hepatic lipid content and thus playing a protective role in prevention of NAFLD.[22] Besides the effect of coffee in prevention of fibrosis and having anti-inflammatory properties; few studies have also established that coffee has a protective role in prevention of hepato-cellular carcinoma.[11,23-25]

In summary, our study was able to support the hypothesis that coffee has a protective role in prevention of NAFLD. Almost all of the studies showing this benefit have been done at a molecular level on rats and mice.

Our study was limited by small sample size and subjective answers to questions in the questionnaire. Further studies with a larger sample size, and possibly long-term prospective studies are needed to better establish the association between coffee and NAFLD.

CONCLUSION

Based on multiple studies done on mice and rat at molecular level and our study, we conclude that various components present in coffee play a significant role in preventing NAFLD, liver fibrosis and even liver cancer. Coffee has also shown to have anti-inflammatory properties and lowers lipid level in blood.

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