Dear Editor,

Please find enclosed a modified version of my Microreview [or high school textbook chapter for the next assignment] manuscript “Title [……]”. To address the concerns and comments raised by the 3 (or 2) reviewers, I made the following changes to improve and clarify the manuscript. It is my hope that these changes make the manuscript acceptable for publication in Microreviews in Cell and Molecular Biology.

Sincerely,

[Savannah Nelson]

**Reviewer 1:**

1. Of the comments made by Reviewer 1, the points regarding my abstract section and adding more topic references into it were very helpful to me and allowed me to improve the quality of my Microreview manuscript

2. In light of comments made by Reviewer 1, I was able to fix some grammatical errors as well as add in another topic sentence better supporting my abstract section with my big picture idea.

**Reviewer 2:**

1. Of the comments made by Reviewer 2, the points regarding potential reformatting of some sentences to better get my ideas across were very helpful and allowed me to improve the quality of my Microreview manuscript.

2. In light of comments made by Reviewer 2, I was able to rewrite some of my sentences that were first confusing. This allowed me to maintain a better flow through my sections and make it easier for the reader.

**Alcohol Consumption and Liver**

**Cancer**

Author: Savannah Nelson  
Major: Biology: Allied Health  
Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

**Key Words:**

Hepatitis C, Hepatitis B, Hepatocellular carcinoma, liver cancer

**Abstract**

**The relationship between alcohol consumption and liver cancer is known to have a correlation. Statistics suggest that frequent alcohol activity later results and aids in the diagnosis of liver diseases such as cirrhosis and further the development of tumors. This field of study is extremely important due to the number of liver cancer patients and their mortality rate. Studies have linked frequent alcohol consumption to the contraction of hepatitis b and c viruses. These viruses are one of the more common links to liver cancer. Future research on the metabolic aspects of this disease association is crucial to developing more positive human practices. Understanding the causes of this cancer more in-depth will provide better scenarios of prevention in the future.**

**Introduction**

Alcoholism is one of the many plagues that has taken countless lives and resulted in detrimental health aspects across the globe. Liver cancer is yet another health ailment that individuals suffer from. In the United States, nearly 15 million people, ages twelve and older, had an Alcohol Use Disorder (Niaaa, 2017). In accordance with this, annually there are 95,000 deaths associated with this addiction. Concerning liver cancer, in 2018, there were 26,875 deaths from this disease (CDC, 2018). Liver cancer often presents with symptoms of upper abdomen discomfort, jaundice, easily bruised or bleeding, weight loss, nausea and vomiting, and more. This disease may be caused by many factors including obesity, infection of hepatitis c or b, hemochromatosis condition, cigarette smoking, or alcohol consumption (CDC, 2021). Interests lie in the correlation between alcohol consumption and the progression of disease of the liver. With such steep statistics individually and linking alcohol consumption as a prior for liver cancer, there must be causation for the two to be credible linked through conducted studies.

**Recent Progress**

In a study regarding overall alcohol consumption frequency and its relation to general health risks, outcomes of such patterns hold great consequences to an individual’s lifetime. Bhautesh J., et al. (2021) selected a cohort size of 309, 123 UK Biobank participants to be questioned about overall alcohol consumption along with frequency, beverage type, and food addition to consumption. Similarly, this study reverenced that of an Italian cohort study which found that drinking wine with food had produced overall lower mortality along with cardiovascular events than those who consume wine without food (Trevisan M. et al. 2001). In addition, nearly 400,000 UK women suggested that through given amounts of alcohol and daily consumption, risks of liver cirrhosis were higher (Simpson R. et al. 2019). This aids in the claim that certain approaches to such consumptions relate to liver cancer prevalence. While taking into account the frequency of the participants in relation to consumption, factors including smoking, physical activity, BMI, blood pressure, cholesterol levels, and C-reactive protein levels were also taken into consideration. While assessing all factors, alcohol consumption was increasing related to mortality and other life-threatening illnesses including cirrhosis and liver cancer. In another study, an approach from the occurrence of hepatitis c related hepatocellular carcinoma comparison was made. Bucci, L. et al. (2016) set out alcoholism and its clinical portrayal on outcomes of Hepatocellular carcinoma as well as the different stages of BCLC or Barcelona Clinic Liver Cancer. Hepatocellular carcinoma is known as the most common primary liver cancer. HCC is the third leading cause of cancer worldwide and in the United States it ranks at number nine (CDC, 2010). Hepatocellular carcinoma is accounted for by 78% of hepatitis b and c viral infections (CDC, 2010). One of the major risk factors for this tumor is frequent copious amounts of alcohol consumption. The prognosis for these patients when the scenario is alcohol related is more commonly grim than in cases non-alcohol related. While one study indicated a larger tumor in addition to an alcohol consumption case, there were other controversial findings when including lower sample sizes. This study included approximately 5,439 individuals who were priorly diagnosed with hepatocellular carcinoma. These participants fell under the category of receiving their diagnosis because of overconsumption of alcohol intake; this was rules by daily intake of >80 g for men and >60g for women over a course of a ten-year period (Bucci, L et al. 2016). The two questions that lead this study were as follows: 1) Does alcoholic etiology affect clinical presentation, treatment and outcome of HCC as compared with tumors associated with HCV infection? 2) Is the effect of alcoholic etiology detectable in all/some BCLC stages? Results were determined by consistent tumor surveillance during an 8–13-month period and entailed severity, management, and overall size. The total number of patients recorded in the results was 2,215 HCC patients. HCC was present in 96.3% of alcohol patients with cirrhotic liver. With fatty liver being the second most common liver disease, there entailed 1.6% of alcoholic cases. Additionally, patients maintain a higher Body Mass Intake and were younger in age by about 4 years of the recorded alcohol cases. Higher accounts of cirrhosis also existed in this result demographic. Concluding these results, the study performed a follow up at near 22 months and retained that 28.3% of the alcohol patients had died (Bucci L. et al. 2016). Similarly, in a study focusing on Wernicke Encephalopathy, alcohol consumption is known to be one of the main risk factors linked to this disease. Wernicke Encephalopathy is caused by a thiamine deficiency and presents itself as a neurological disorder. Along with the adaption of liver disease, Wernicke Encephalopathy patients are made up of 90% of individuals suffering from Alcohol Use Disorder (Novo 2021). This study approached the relation between liver disease and Wernicke Encephalopathy because its relationship relevance is unclear. Through their surveying, finding indicated that patients who also had liver cirrhosis, hepatitis c, and hepatitis b viruses made up a percentage of alcohol dependent Wernicke Encephalopathy patients. These three studies all signify a correlation between frequent alcohol consumption and liver related diseases and liver cancer.

**Discussion**

These studies all present findings that show a causation and relationship between overconsumption of alcohol on a more than frequent basis and the development of liver diseases and liver cancer. These identified relationships help us to understand the causes of liver cancer and ways of preventing a diagnosis, to a certain extent. While genetics has the biggest influence on cancer, most of what is put into the body is extremely impactful to overall health and the future of an induvial. There is still research to be done to further identify what mechanisms biologically and on a pathophysiological level can alter the body’s make-up and allow for DNA mutations. Along with narrowing out other causing factors of liver cancer, there will be more confidence in this relationship and greater cause for correlation between alcohol consumption and liver cancer. Holes found in these studies were mainly on the basis of conflicting standard diagnosis criteria. There are many causes for most diseases, therefore discovering a participant pool without bias and other concerning life factors can occasionally be a challenge. Mainly, underlying mechanisms of identified connections remain unknown and serve as limitations to studies in this topic field.

**References**

L. Bucci, F. Garuti, V. Camelli, B. Lenzi, F. Farinati, E. G. Giannini, F. Ciccarese , F. Piscaglia, G. L. Rapaccini, M. Di Marco, E. Caturelli, M. Zoli F. Borzio, R. Sacco, M. Maida, M. Felder, F. Morisco, A. Gasbarrini, S. Gemini, F. G. Foschi, G. Missale, A. Masotto, A. Affronti, M. Bernardi, F. Trevisani & for the Italian Liver Cancer (ITA.LI.CA) Group12016. Comparison between alcohol- and hepatitis C virus-related hepatocellular carcinoma: clinical presentation, treatment, and outcome. Alimentary Pharmacology and Therapeutics. 43:385-399.

Bhautesh Dinesh Jani, Ross McQueenie , Barbara I. Nicholl, Ryan Field, Peter Hanlon, Katie I. Gallacher, Frances S. Mair and Jim Lewsey. Association between patterns of alcohol consumption (beverage type, frequency and consumption with food) and risk of adverse health outcomes: a prospective cohort study. BMC Medicine. 19:8 pages 1-14.

Ignacio Novo-Veleiro a,1 , Javier Herrera-Flores b,1 , Beatriz Roson-Hern ´ andez ´ c , Jos´e-A. Medina-García d , Roberto Muga e , Joaquín Fernandez-Sol ´ a´ f , M.-Candelaria Martín-Gonzalez ´ g , Elena Seco-Hernandez ´ h , Carlos Suarez-Cuervo ´ i , Ana-M. Mateos-Díaz j , Rafael Monte-Secades k , Begona ˜ Machado-Prieto l , Rub´en Puerta-Louro m, Cristina Prada-Gonzalez ´ n , Alvaro ´ Fernandez-Rial ´ o , Patricia Sabio-Repiso p , Rocío Vazquez-Vigo ´ q , Ana-C. Antolí-Royo r , Aina Gomila-Grange c , Nieves-C. Felipe-P´erez d , Arantza Sanvisens-Berg´e e , Emilia Antúnez-Jorge f , Camino-M. Fern´ andez-Rodríguez g , Lucía Alvela-Suarez ´ s , Alba Fidalgo-Navarro i , Joaquín Castro t , María-A. Polvorosa-Gomez ´ u , Mario Del Valle-Sanchez ´ v , Jos´e Lopez-Castro ´ w, Antonio-J. Chamorro b,2 , Miguel Marcos b,\*,2 , on behalf of the Wernicke-SEMI Group, Alcohol and Alcoholism Group, Spanish Society of Internal Medicine (SEMI). 2021. Alcoholic Liver Disease Among Patients with Wernicke Encephalopathy: A Multicenter Observational Study. Drug and Alcohol Dependence in Science Direct. 230:109816 pages 1-6.

2018-2019, Alcohol Facts and Statistics. National Institute on Alcohol Abuse and Alcoholism. https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/alcohol-facts-and- statistics

January 19, 2021. Liver Cancer. Center for Disease Control and Prevention. https://www.cdc.gov/cancer/liver/index.htm

May 7, 2010. Hepatocellular Carcinoma: Morbidity and Mortality Weekly report. Center for Disease Control and Prevention https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5917a3.htm

Trevisan M, Schisterman E, Mennotti A, Farchi G, Conti S. Drinking pattern and mortality:: the Italian Risk Factor and Life Expectancy Pooling Project. Ann Epidemiol. 2001;11(5):312–9

Simpson RF, Hermon C, Liu B, Green J, Reeves GK, Beral V, et al. Alcohol drinking patterns and liver cirrhosis risk: analysis of the prospective UK Million Women Study. Lancet Public Heal. 2019;4(1):e41–8.