Dean&Francis

ISSN 2959-409X

Racial Disparities in Primary Liver Cancer Death

Dongyi Jiao

Clinical Medicine & Biomedical Science, Nanchang University, Nanchang, China

jp4217121239@qmul.ac.uk
*Email:

Abstract:

Primary liver cancer is one of the four leading causes of cancer death in humans, and the ethnic diversity and wide distribution of the affected population are very serious, so it is important to control the mortality rate of primary liver cancer patients worldwide. In order to control the global proportion of patients with liver cancer and reduce the mortality rate of primary liver cancer, it is necessary to identify the differences between ethnic groups and explore the impact of these differences on the prevalence of primary liver cancer. Diet and genes make Spain and blacks in Europe and the United States more susceptible to liver cancer, while the culture and lifestyle of Asia make people in Central Asia and Southeast Asia more susceptible to hepatitis virus infection and non-alcoholic hepatitis (NAFLD). The specific activation temperature of Aspergillus flavus causes it to secrete aflatoxins in tropical and subtropical regions, and its exposure to the toxin can carry HBV infection and increase liver cancer's prevalence in local residents. Gender is also a main factor of liver cancer's mortality differences, which is mostly due to the fact that men have a higher proportion of smoking, alcohol abuse and overweight. This means that in countries with a high proportion of men, such as the U.A.E., Qatar, the Philippines and other Southeast Asian regions, the prevalence and mortality of liver cancer will be higher.

Keywords: Primary liver cancer; racial disparities; toxic metal; hereditary hemochromatosis.

1. Introduction

Primary liver cancer is one of the fourth leading cause of global cancer death and one of the sixth most commonly diagnosed cancer globally. The two main categories based on histology is hepatocellular carcinoma (3/4of all liver cancers) and intrahepatic cholangiocarcinoma (15% of all liver cancers) [1,2]. Patients with cirrhosis and liver disease are more likely to develop primary liver cancer, with significant differences in the likelihood of developing primary liver cancer among patients from different countries due to different etiologies [1,3]. By analyzing the sources of such differences and the pathogenic mechanisms, scholars will be more likely to carry out targeted treatments, and national and local

governments will be able to formulate relevant policies to promote targeted drugs and control the pathogenic environment, thereby reducing the mortality and morbidity of primary liver cancer, while reducing the cost of treatment and reducing the pressure on medical institutions and patients' families. This review systematically introduces the differences in mortality caused by primary liver cancer among different ethnic groups, and discusses the various reasons that contribute to these differences.

2. Current Situation of Primary Liver Cancer

Although in some East Asian countries have decreasing incidence and mortality of primary liver cancer, such as China, Korea and Japan, the incidence has increased in many countries of the world with previously low incidence in several European countries and North American countries [4]. Population ageing, gender factors (men are at higher risk than women), and ethnicity are all risk factors for liver cancer in humans [5]. In countries with multiracial populations, such as United States, non-Spain whites have lower rates than Asian/Pacific Islander, Indians, Spain, and non-Spain blacks [5,6]. Although the proportion of overweight and obesity in Europe and the United States is much larger than in Asia and Africa, Asia has the highest prevalence of liver cancer, while Africa has the steepest mortality rate. The reason for this is that studies have found that Asians are more susceptible to hepatitis virus, and the genetic sequences of HBV and HCV are more compatible with those of Asians and are more easily recombinant, while African countries have insufficient development and economic capacity to support the follow-up treatment of liver cancer patients, resulting in extremely high mortality rates [7]. For people in North America, especially Caucasians, their diet, lifestyle and genes lead to their obesity-prone physique, and after being overweight and obese, not only the liver is overloaded, but also many problems will occur in other organs. Therefore, before liver cancer, there are usually other diseases such as hyperlipidemia and heart disease, which relatively reduce the proportion of liver cancer. In the past two years, a research team has collected relevant data, and in 2020, about 0.9 million people were diagnosed with liver cancer in the world, and as many as 830,000 patients died from liver cancer, of which East Asian patients accounted for more than half, and the proportion of deaths alone was as high as 54.1% [8]. Also in 2020, the population of East Asia was about 1/5 of the global population, yet China itself accounted for 45% of the liver cancer cases worldwide and nearly half of the global total deaths [8].

In addition to the internal differences of human beings, the differences in the external environment are also important factors affecting the development of liver cancer in different ethnic groups. The most significant exogenous causative factors are viral infections, mainly HBV and HCV. In addition, excessive alcohol consumption, smoking, aflatoxin intake, and metabolic diseases (type 2 diabetes , non-alcoholic fatty liver disease) are also major contributors to form and determine the liver cancer. However, these risk factors for liver cancer are preventable, and liver cancer's primary prevention is very important to reduce the global burden of liver cancer in the future.

3. Epidemiologic and Lifestyle Risk Factors for Liver Diseases

According to statistics, patients with primary liver cancer due to chronic HBV infection account for more than 50% of liver cancer patients worldwide, and hepatitis cancer caused by HBV is most common in South Africa, Central Asia and Southeast Asia [9,10]. Hepatitis B vaccine has been introduced in more than 100 countries and regions, with a three-dose coverage rate of more than 80% and is expected to exceed 90% [11]. Prevention of HBV infection through neonatal immunization can significantly prevent the prevalence of HCV-induced liver cancer. The Shanghai study showed that the morbidity of liver cancer among young people who were vaccinated as an infant decreased by 54% compared to the same age group among unvaccinated people, demonstrating the effectiveness of the hepatitis B vaccine rollout policy [12].

Another virus that can cause liver cancer is HCV, which accounts for one-fifth of all patients worldwide due to HCV infection. There is no HCV vaccine, but HCV infection can be treated with specific antiviral drugs, thereby reducing the global spread of HCV [13]. In response to the trend of reducing hepatitis virus infections, the World Health Organization (WHO) set a target in 2016 to reduce HBV and HCV-related mortality, with a 65% reduction in mortality from both viruses by 2030. Therefore, achieving universal vaccination of HBV vaccine and making antiviral drugs widely available are key to achieving the WHO2030 target [14].

Nonalcoholic fatty liver disease (NAFLD) is a usual chronic liver disease form, which is more common in developed countries in United States and the Europe. It is further divided into nonalcoholic steatohepatitis (NASH) and non-alcoholic fatty liver disease (NFAL) according to the histological characteristics of the liver, which are significantly related to liver fibrosis, and persistent disease and disease progression can progress to cirrhosis and

ISSN 2959-409X

even hepatocellular carcinoma. Risk factors for NAFLD include type 2 diabetes, obesity, and metabolic syndrome, which are strongly associated with lipid accumulation and oxidative stress, which are genetically linked to European and American populations. Therefore, the daily diet and exercise of the risk groups in Europe and the United States need to be controlled and maintained, and at the same time, it is also necessary to pay attention to whether there are related genetic diseases in the family history, and genetic screening should be carried out as soon as possible to do a good job in prevention and early treatment. The development and use of new targeted drugs to regulate lipid degradation and oxidative stress related pathways to improve NAFLD may provide a new way of thinking and a new way to treat this disease. However, the potential mechanisms and practical applications are not yet mature and require further research and human simulations of retrograde.

Aspergillus flavus is a fungus that can enter the human body by contaminating crops and accumulate aflatoxins to cause liver cancer. Due to the fact that aspergillus flavus produce the highest amount of toxins in environments with sufficient oxygen, temperatures between 33-38 ℃, and weak acidity (which is common in tropical and subtropical regions), and are less prone to toxin production and activation under other conditions, aflatoxin is classified as an epidemiological category rather than an environmental toxin factor. Aflatoxins can cooperate with HBV infection and increase the possibility of liver cancer, so it is necessary to properly preserve crops, and relevant departments should also improve the hygiene and quality inspection of crops to reduce the number of people suffering from liver cancer due to aflatoxin exposure. Other life risk factors that can easily lead to liver cancer include smoking, excessive alcohol consumption, and the government can control the harm of these risk factors to the human body by raising taxes on tobacco and alcohol, reducing product promotion, and banning alcohol and smoking in some areas. At the same time, medical insurance is formulated, relevant examinations are provided free of charge, and medical expenses are partially reimbursed, which reduces the economic pressure of patients and reduces the operational burden of medical institutions. Compared with the pathogens and the negative impact of the external environment on the human liver, people‘s lifestyle has a great impact on liver cancer, long-term drinking, staying up late, greasy diet will lead to liver overload and visceral fat accumulation, which will lead to a series of liver diseases, primary liver cancer is the ultimate and worst form of the disease. The prevalence of alcohol-associated liver disease (ALD) has increased dramatically due to the increase in alcohol consumption in society. Statistically, the full-spectrum prevalence of ALD was 4.1% in whites, 3.4% in blacks, 9.3% in Spain, and 2.7% in other participants. Spain and black populations have higher ALD compared to white populations. This is not only because of the increased burden of disease due to the higher density of alcohol stores in Spain and black-populated areas, but also because the patatin-like phospholipase domain-3 (PNPLA3) gene is strongly associated with liver fat content and hepatocellular injury, and the PNPLA3 gene is more dominantly expressed in Spain and black ethnicity [7]. People who stay up late for a long time also have a very high risk of liver cancer. Staying up late will lead to negative effects such as hormone metabolism disorders, liver cell damage, and liver toxin accumulation, and reduce human immunity, making the body more susceptible to pathogenic infection, leading to fatty liver and viral hepatitis, thereby increasing the incidence of liver cirrhosis and liver cancer. In Asia, such as China, Japan and other countries, there are a large number of young people who stay up late to work with chronic liver disease, and long-term untreated leads to the formation of liver cancer. Therefore, it is necessary to reduce lifestyle risk factors, maintain a healthy routine and reasonable eating habits as the first condition.

4. Toxic Environmental Chemicals and Liver Disease

Setting aside disease screening and staging, strict monitoring of the environment is also beneficial for reducing the incidence and mortality of liver cancer. Industrial pollution leads to a large amount of environmental pollution, among which metals cause significant damage to the liver. Workers in factories and residents near discharge areas have the greatest threat of illness. Long term pollution can cause the entire sea area and region to be covered by toxic substances, resulting in widespread human harm. For example, iron in sewage can be recycled again if not filtered properly and enter the human body through drinking water and food. When overconsumption occurs, it does not only leads to hereditary hemochromatosis (HH), but also chronic hepatitis and non-alcoholic fatty liver disease, all of which indirectly promote the formation of liver cancer and greatly increase the risk of disease [15]. In 2021, an academic group calculated that HH patients were 20 to 200 times more likely to develop liver cancer, eventually leading to the death of 45% of HCC patients [16]. In China‘s sewage discharge control policies, it is clearly stated that water bodies for different purposes are divided, and industrial wastewater can only be discharged into specific water bodies, which undergo rigorous sediment and metal

filtration, and are separated from water bodies that supply drinking water to the public, and are not considered as drinkable water sources. This policy greatly reduces the possibility of people increasing the incidence of liver cancer through excessive intake of iron, and the incidence of many parasitic diseases and other metal poisoning diseases has also significantly decreased.

5. Gender Differences

Statistics on the proportion of liver cancer death in the first 30 years, it is found that most of the liver cancer cases are aged between 50 and 54 years old in men and 65 to 69 years old in women, and the prevalence and mortality rate of women in these 30 years is greater than that of men, and the prevalence rate of men is more than three times that of women, which is related to the proportion of smoking and alcohol abuse in men is much greater than that of women [17]. In European and American countries represented by United States, overweight in men and obesity in women are very common due to diet and lifestyle, which increases the incidence of hyperlipidemia in the population. In Central Asian countries represented by China, HBV infection and high intake of cheap alcohol led to the formation of liver disease, and liver cancer occurs due to long-term untreated or ineffective treatment of liver disease. Therefore, for people of different genders, different BMI standards should be paid attention to, and overweight and obese people should pay attention to their diet and lifestyle habits, including occupational factors and racial factors. Since the morbidity and mortality rate is higher in men than that in women, men should be regarded as the key prevention and control group in the future, and higher standards should be set for the quantity and quality assurance of tobacco and alcohol sales, and their publicity and sales should be restricted.

6. Conclusion

In 2020, there were about 900,000 liver cancer patients worldwide, of which more than 800,000 died due to liver cancer. Primary liver cancer is one of the most common cause of cancer death in many countries, and East Asia has the highest mortality rates of liver cancer. Under the premise of controlling the mortality of liver cancer, scholars predict that the number of new cases and mortality of liver cancer will increase by more than 50% by 2040. Therefore, in order to achieve a reduction in the burden of illness and medical stress, it is necessary to control the incidence rate by at least 3% per year. However, the prevalence and mortality of liver cancer have not decreased significantly in recent decades, so the primary prevention of liver cancer is the first measure to reduce liver cancer's global burden. The pathogenic factors of liver cancer are complex, and they are divided into three categories: lifestyle risk factors, environmental toxicant factors and gender differences according to different ethnic groups, and different methods are used to prevent and regulate different categories, analyze the past pathogenic causes and predict the future after taking control measures, set ideal targets for liver cancer prevalence and mortality, continuously monitor the feasibility and effectiveness of national and local policies, and continuously optimize population control and education, so as to gradually reduce the impact of primary liver cancer on humans. However, this article does not discuss the impact of population aging and future changes in sex ratio on disease, and although it is predicted that the prevalence and mortality of primary liver cancer will decrease in the future, it is still necessary to focus on the elderly and male groups through better prevention and treatment strategies.

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