

Racial Disparities in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is a leading cause of cancer mortality worldwide and represents a growing number of cancer deaths in the United States.¹ Similar to other malignancies, disparities in management and survival exist for patients with HCC based on race and other socioeconomic characteristics. The incidence of HCC is higher for Black patients.² After diagnosis, Black patients are less likely to receive surgery, wait longer for surgery, and have worse overall survival.³ Patients with low income who are underinsured or uninsured face similar disadvantages.

Some of these disparities are provider-based. Patients with HCC who are treated at safety-net hospitals are less likely to undergo surgery, and those who do receive fewer liver transplantations or resections and undergo more ablation procedures.⁴ Surgery is also less common at community versus academic cancer centers.⁴ However, hospital variation does not fully explain the observed survival inequities.

In this issue of *Cancer*, Shaltiel and colleagues deliver a thoughtful investigation of racial differences in HCC presentation.⁵ By using a modern series of patients from a high-volume academic institution, the authors compared Black and non-Black patients who had a history of hepatitis C and were diagnosed with HCC. Black patients had better liver function, lower α -fetoprotein levels, and less fibrosis/cirrhosis according to several measures. Despite this advantage, they presented with more advanced HCC. Black patients were less likely to meet the Milan criteria and more likely to have bilateral, multifocal, poorly differentiated, and metastatic tumors.

Noting the increased rates of hepatitis B and human immunodeficiency virus (HIV) exposure and infection among Black patients, the authors performed subset analyses of HCC presentation for Black and non-Black patients with and without these concurrent conditions. Regardless of hepatitis B and HIV status, Black patients still had less advanced liver disease but more advanced tumor characteristics.

Countless studies have correlated advanced cancer presentation with minority race, lack of health insurance, or low socioeconomic status. A common explanation for these findings is the barriers to health care experienced by vulnerable populations. Patients with limited resources are less likely to participate in cancer screening or even to present when they develop concerning symptoms. Other hypotheses include differences in diet, lifestyle, cultural factors, and medical comorbidities.⁶

Racial differences in tumor biology are often suggested but poorly understood. Triple-negative breast cancer, which has fewer treatments and a worse prognosis than other tumors, is more common among Black women.⁷ Prostate cancers in Black men have increased inflammation and unique genetic mutations that correlate with inferior survival.⁸ The interesting and novel aspect of the current study is that advanced HCC presentation among Black patients was independent of known and measurable risk factors, such as fibrosis, cirrhosis, and coinfection with hepatitis B, hepatitis C, or HIV.

In light of these observed differences in disease presentation, the authors suggest that we revise the current surveillance criteria for HCC to account for this increased risk. They suggest screening all Black patients with a history of hepatitis C exposure, regardless of cirrhosis. Such a change could reduce disparities suffered by Black patients with HCC, with earlier diagnosis and more treatment options.

Still, we must dig deeper to understand the causes of these disparities. There is a growing body of evidence suggesting that unique genetic mutations increase cancer risk among patients of African ancestry.⁹ With regard to HCC, there appears to be a strong connection to epigenetic factors as well.¹⁰ Variations in cytochrome p450, glutathione-S transferases, and other enzymes influence the ability to detoxify known hepatic carcinogens, many of which are chemical or industrial agents.¹¹

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Dietary and lifestyle factors also play a role. Diabetes, obesity, and hepatic steatosis are all correlated with an increased risk of HCC.¹² Combined with hepatitis C, alcohol and tobacco use have a synergistic effect increasing HCC risk.^{13,14} Variation in N-acetyltransferase 2 activity has been demonstrated among patients of certain African ancestries compared with European and Asian populations,¹⁵ and such polymorphisms are associated with differing HCC risks because of diet.¹⁶

Of course, *race* is more than genetics. It has been suggested that the drivers of racial disparities are more social than biologic.¹⁷ Indeed, racial inequity in exposure to the aforementioned HCC risk factors is well documented and has stemmed from years of racist laws and policies.

A combination of federal and local housing policies, combined with discriminatory lending and other racist practices in the private sector, have created a pattern of residential segregation and wealth inequality across the United States.¹⁸ Many Black communities were saddled with low property values and loose zoning policies that attracted industrial activity and subsequent pollution. This disproportionate exposure to hazardous waste, aromatic chemicals, lead poisoning, and other toxins contributes to worse health outcomes among Black patients.¹⁹

Residential segregation has also left many urban communities without access to healthy and affordable nutrition. Black families are twice as likely as white families to live in a food desert.²⁰ and dietary risk factors for HCC are more prevalent in these malnourished communities. Government programs that reduce inequities in housing, pollution, and nutrition could improve outcomes for HCC and numerous other conditions.

Researchers investigating racial disparities in health care must no longer accept *biologic differences* as an explanation. This common conclusion is inaccurate and apathetic. When significant disparities exist, there is a reason. It is also increasingly important to take a translational approach to clinical and health services research. Shaltiel et al have performed a thorough analysis that identifies a discrete racial disparity in HCC presentation.⁵ Armed with this understanding, they suggest a targeted policy adjustment to improve outcomes. More studies should follow this example. We must start creating solutions rather than simply identifying problems.

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