

Long Covid, A Hidden Public Health Challenge: How It is Impacting Lives At A Local Level Based on Clinic Experience in Rural South Carolina

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Introduction

The long-term effects of COVID-19, commonly referred to as "long covid," have become more popular in recent years as a substantial number of individuals report lingering symptoms long after their initial infection. These symptoms can range from coughs, fatigue, and shortness of breath to neurological and cognitive impairments, affecting various aspects of patients' health and quality of life. While numerous studies have examined the short-term effects of COVID-19 on immune function and organ systems, there is limited research exploring the potential long-term consequences on cancer development. Given that COVID-19 affects immune responses, and inflammation levels, it is also plausible that the virus may have a role in increasing the risk of malignancies in some individuals. We examined patient data that includes reports of COVID-19 infection, symptom persistence, and subsequent cancer diagnoses. By identifying patterns and correlations between these factors and patient labs, scans, and diagnoses, we aim to contribute valuable insights into the broader understanding of Long Covid and its potential impact on cancer risk.

Long Covid is a complex, multi-organ illness that occurs in individuals with a history of SARS-CoV-2 infection, with onset and persistence occurring usually 3 months from the onset of COVID-19 with symptoms that last for months or years and cannot be explained by an alternative diagnosis (WHO). It is believed that Long Covid typically results from ongoing inflammatory changes in multiple tissues¹. The Long Covid patients require need for multiple specialists. Long Covid is likely to impact 80% of those infected with history of SARS-CoV-19 infection with at least one symptom and can linger on. Fatigue is the most reported symptom of Long Covid². More severe cases involve damage to a variety of organ systems primarily from ongoing inflammatory processes in the lungs, heart, nervous system, kidneys, and liver, thrombotic and cerebrovascular disease, type 2 diabetes, myalgic encephalomyelitis/chronic fatigue syndrome dysautonomia, postural orthostatic tachycardia syndrome (POTS) as well as along with mental health impairment³⁻⁴. The pathophysiological pathways may involve direct consequences of the post infectious inflammatory or autoimmune responses⁵. More than 200 symptoms have been identified to be associated with long COVID. It is also believed that Long Covid triggers 25% increase in prevalence of anxiety and depression worldwide⁶.

Long Covid and Cardiovascular disease⁷⁻¹¹

Long Covid patients with cardiac involvement have persistent dyspnea, fatigue, chest pain, and cough. These symptoms impact approximately in one out of five patients 3 months after the acute SARS-CoV-2 infection¹². In the general population, Long Covid associated cardiac inflammation is reported in 150 cases per 100,000. The risks of myocarditis and pulmonary embolism are reportedly higher than most of the other cardiovascular complications¹³.

Neurological complications with PASC¹⁴⁻¹⁴

Neurological manifestations of Long Covid is observed in 33% of patients with Long Covid. These manifestations can impact either the central or peripheral nervous system. The most frequent symptoms include fatigue, "brain fog", headache, cognitive impairment, sleep, mood, smell, or taste disorders; muscle aches. Cognitive dysfunction impacts attention, problem solving, and decision making. Memory impairment involves both the short and long-term memory. Younger people (16–30 years old) suffer potentially severe symptoms, such as concentration and memory problems, persistent 6 months after infection. The study of the anatomical or functional imaging of brain alterations in Post-Acute Sequelae of COVID-19 (PASC) shows consistent changes in many brain areas. A pronounced loss of gray matter was also as well also an increase in cerebrospinal fluid (CSF) volume and decrease of whole brain volume respect to the controls, suggesting an additional diffuse loss of gray matter. Covid-19 is a risk factor to develop dementia, neurodegenerative diseases and mild cognitive impairments even in 50-year-old adults.

Other major health issues associated with Long Covid¹⁵⁻¹⁶

Many symptoms that persist (in addition to disease specific) 1 year after the acute disease included cognitive and mental health disorders, such as depression, anxiety, memory loss, concentration difficulties and insomnia, fatigue, dyspnea, muscle, and joint pain and ongoing inflammation. One prospective study of low-risk individuals, looking at the heart, lungs, liver, kidneys, pancreas and spleen, noted that 70% of 201 patients had damage to at least one organ and 29% had multi-organ damage. In one year long study of patients with long Covid research group with authors found that 59% had single-organ damage and 27% multi-organ damage. Another study of renal functions from Veterans infected with Covid 19 reported an increased risk of numerous damage to kidneys

Long Covid, Inflammation and cancer¹⁷⁻²⁴:

The oncogenic potential of viral infections is well known since the discovery of Epstein-Barr Virus (EBV) and lymphoma since early sixties. Approximately 15%-20% of all cancer cases can be attributed to carcinogenic viral infections. At least seven different human cancer oncogenic viruses have been shown to have strong connections to various forms of cancer in humans, including the Epstein-Barr virus, human papillomavirus and the hepatitis B and C viruses.

The molecular oncogenic mechanisms from viral infections are varied. These mechanisms range from chronic inflammation to immunosuppression and DNA modification alteration in mitochondrial function, methylation, functioning as external oncogenes, over-activating human oncogenes and/or inhibiting tumor suppressors.

Chronic inflammation has been identified as an important step in tumorigenesis. For oncogenic viruses to develop cancer must develop mechanisms that help them to evade host immune systems. Second, persistent infections must be capable of inducing mild but persistent inflammation explains their oncogenic potential. Chronic inflammation increases the generation of mutations and will consequently increase the risk of tumor development.

Long Covid is essentially associated with activation of the inflammatory pathways. Within 6-8 weeks of SARS-coV-2 infection, a significant inflammatory response is observed. In addition, mild or asymptomatic patients have demonstrated neutrophil dysfunction, which in turn increases susceptibility to cancer.

Another potential mechanism may be the "reactivation" of SARS-CoV-2 or other viruses. The residual virus cells could result in long-lasting immunomodulatory effects. This may explain the low-grade inflammation. This chronic inflammation coupled with oxidative stress could lead to tissue and DNA damage.

Another mechanism in Long Covid, inflammation and cancer may come from the SARS-CoV-2 spike protein which contains a furin-like cleavage site. This spike protein promotes the activation of the NLRP3 inflammasome and NF- κ B inflammatory pathways. Elevated inflammasome pathways may increase oncologic potential. In summary, in addition to chronic ongoing inflammation, Long Covid may be likely be a risk factor for new cancer by following different mechanisms.

- Chronic Virus Infection, Residual Virus Proteins and Cancer Risk
- Chronic Inflammation from Long Covid
- Cell senescence
- The Oncogenic Potential of SARS-CoV-2
- Immunosuppression

Long Covid's Impact on Disparities²⁵⁻²⁸:

RECOVER program sponsored by the NIH for Long Covid has revealed that Black and Hispanic Americans appear to experience more symptoms and health problems related to long COVID compared to Caucasian patient population. This evidence suggests that there are important differences in how long COVID manifests in different racial and ethnic groups. Among non-hospitalized COVID-19 patients, Hispanic individuals had higher adjusted odds of being diagnosed with Long Covid across 6 of 8 organ systems. Black individuals had higher odds of diagnosis across 4 of 8 systems. Black patients had twice the risk of diabetes, and one-and-a-half times the odds of being diagnosed with chest pain in Long Covid. These differences may be explained due to interacting biological, environmental, and social factors. Immunogenetic differences also exist among populations, affecting the immune cell repertoire and resulting in racial differences in immune profiles. African Americans are significantly more likely to carry genetic variants of proinflammatory cytokines. Furthermore, aggravatingly, they often bear genotypes (including variants of IL-1, IL-6, IL-10, and TNF- α) known to tamp down the anti-inflammatory responses leading to more inflammatory diseases that are more common among African Americans leading to consequential Long Covid.

Population Health Impact with Long Covid²⁹⁻³¹

With more than 600 million individuals infected with Covid-19 it is estimated that least 65 million individuals around the world have long COVID, based on a conservative estimated incidence of 10% of infected people. In the USA over 100 million COVID infections have occurred by the fall and winter of 2022-23 in the USA. With estimated 15-30% of those infected will develop Long COVID, it is postulated that 7% or close to 15 million Americans have been impacted by long COVID. Long COVID outpaces Diabetes in terms of cost per member for a given health plan (Beckers Payer). Long COVID is associated with all ages and acute phase disease severities, with the highest percentage of diagnoses between the ages of 36 and 50 years, and most long COVID cases are in non-hospitalized patients with a mild acute illness.

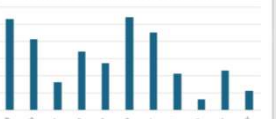
We at the Carolina Blood and Cancer Care, Community Clinical Oncology Network (CCOON) and No One Left Alone (NOLA) are working on identifying all aspects of Long Covid in our patient's population in Rural South Carolina (supported by the SC state financial support).

In addition to examining the direct correlation between long COVID and cancer diagnoses, this study also investigates the role of social determinants of health (SDOH) in shaping these outcomes. Social factors such as income, gender, education, and race can significantly influence the severity of COVID-19 symptoms, the likelihood of long-term health complications, and overall patient outcomes. By comparing patients from diverse socioeconomic backgrounds and with varying SDOH, we aim to identify how these factors may exacerbate the effects of long COVID and contribute to disparities in cancer diagnoses among affected populations.

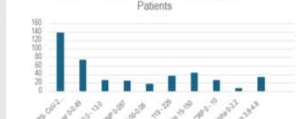
Summary

This ongoing research presents a compelling case for the urgent need to investigate the intricate relationship between Long COVID, inflammation, heart disease, brain fog and cancer. As leading oncologists as well as a group of population health experts and a team of dedicated scientists from across the world (see the list at the end), we recognize the potential implications of this emerging health crisis and the impact it may have on patients' long-term well-being. By analyzing various aspects such as cardiovascular disease, neurological complications, health care disparities, and the impact of long COVID on chronic comorbidities, we aim to shed light on the broader population health impact of this condition. Additionally, we explore the role of COVID-19, mitochondria, miRNA, methylation, and viruses in the context of cancer development and the associated healthcare costs. Finally, we examine the trends in new cancer patients among community cancer patients before and after the COVID-19 pandemic. By shedding light on these interconnected areas, we aim to encourage oncologists and pharmaceutical companies to support research efforts and collaborate in seeking effective treatment for this complex condition.

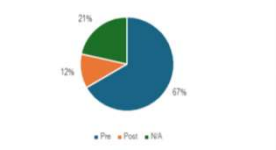
Long Covid Symptoms Reported by Patients



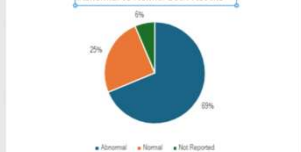
Count of Abnormal Labs for 150 Long Covid Patients



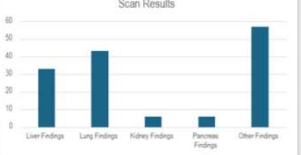
Cancer Diagnoses Pre or Post Covid Infection



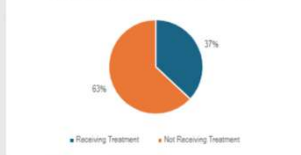
Abnormal vs Normal Scan Results



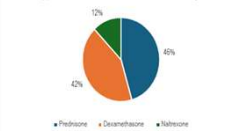
Distribution of 97 Long Covid Patient Abnormal Scan Results



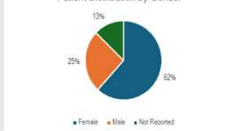
Long Covid Patients Receiving Treatment



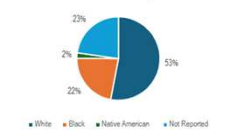
Type of Treatment Patients are Receiving



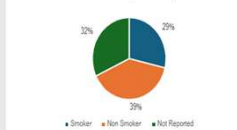
Patient Distribution by Gender



Patient Distribution by Race



Patient Distribution by Smoking Status



References

Scan this QR code then select "View PDF" to view all references.

