Disparate Biosocial Risk of Malaria and Sickle Cell Disease in The United State

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Human malaria is caused by parasites in the genus *Plasmodium*, which are vectored by female *Anopheles* mosquitoes. Malaria disproportionately affects the Sub-Saharan African region, whose population has had historically limited access to fair and equivalent healthcare as compared to Western regions.[1] Sickle cell disease (SCD), a known population scale consequence of malarious countries,[2] is a condition wherein abnormally shaped red blood cells inhibit mosquito feeding, therefore providing protection against *Plasmodium* infection and subsequent development of malaria.[3] The presence of SCD in the United States can be traced to global imperialism that led to the forced movement of peoples from African malarious countries for purposes of enslavement in growing colonies.[4] Current patterns demonstrate a disproportionate burden of SCD in Black and African Americans, further emphasizing the medical and biosocial isolation experienced by this subpopulation in the United States.

Malaria is endemic throughout Africa, due in part to optimal climate and habitat availability for Anopheline mosquitoes.[5] The disease presentation of malaria in humans is categorized as either uncomplicated or severe. Uncomplicated malaria presents with flu-like symptoms, such as fever, chills, nausea, and vomiting.[5] Severe malaria can present as a variety of conditions such as acute respiratory distress, low blood pressure, abnormal behavior, seizures, or acute kidney injury.[5] A diagnosis of malaria usually requires a blood sample from patients to either detect the parasite itself or related antigens. Accurate diagnoses can be hindered in resource poor regions where laboratory facilities and trained personnel may not be available, as well as different species of malaria parasite present which accumulate at varying rates in the blood, present differing antigens, and initiate various immunological responses.[6] Delayed diagnosis delays appropriate treatment, which severely inhibits positive patient outcomes and has been identified as the primary cause of malaria-related death in many countries of Sub-Saharan Africa.[5,6]

American Burden of SCD

There are an estimated 100,000 Americans with sickle cell disease, and more than 3,000,000 who are heterozygous carriers of the HbS allele that causes the disease.[3,6] Originally, this genetic mutation offered protection to those who had diagnosable SCD, but also to those known as sickle-cell trait (SCT) carriers, people who possessed a heterozygous combination of one recessive SCD gene and one functional hemoglobin gene.[7] In fact, SCT carriers had up to 60% protection from malaria, even without presenting SCD traits.[7,8] Both homozygous recessive and heterozygous presentations of the HbS allele created protection for those living in malarious regions, but this benefit has disappeared as those carrying the sickle-cell trait have migrated to malaria-free regions. Sickle cell has continued to persist despite the negation of these protective advantages, leaving individuals in areas such as the U.S. solely with the socio-physical complications presented by the disease.

From the 1500s to the mid-1800s, at least 10 million African people were forcibly displaced by African slavers, an event known commonly as the Trans-Atlantic Slave Trade.[9,10] When comparing maps of malarious countries and where displaced African populations originated, there are observable patterns in which the majority of the population originated in malaria endemic regions, where the evolutionary pressure of malaria contributed to the long-term development of SCD in the population.[11] In the Americas, much of the contemporary SCD prevalence is directly due to the Trans-Atlantic Slave Trade.[12] Although the risk of contracting malaria is low in the USA,[12] the prevalence of SCD is high, particularly in the Black and African American communities.[7,13] This relationship draws attention to the unidentified cause of the persistence of SCD in this community and the potential for relieving burden.

The conferred advantage granted from SCD to malaria leads to logical and observable patterns of areas with high malaria prevalence coinciding with areas of high SCD prevalence (see, for example, references 14 and 15). With mass underreporting in Africa, it is hard to determine the true historical and modern burden of SCD in malarious countries.[16] Although data shows deaths attributable to SCD in Africa have increased 26% since 2000, this number may be even higher.[17] The direct connection between malaria endemic regions presenting higher prevalence of sickle cell anemia decreases in more recent decades as data sampling has increased in validity and become more representative.[16] More specifically, prevalence of SCD in non-malarious regions has been seen to decrease recently due to consistent early intervention in sickle cell patients.[17] *In-utero* diagnosis of SCD is possible by sampling amniotic fluid of the mother's womb, and infants can be tested at birth before symptoms appear.[18] When early diagnosis procedures are in place, rapid treatments are possible, which can dramatically increase the life expectancy, quality of life, and overall health of those who suffer from SCD. In some cases, there is record of the disappearance of sickled cells in patients who receive stem-cell transplants early in life.[19] However, many health clinics in malarious regions lack technology, services, and funding to be able to provide ample quality care. In 2020 alone, 95% of the 627,000 deaths occurred in the WHO's Africa region, an under-resourced region that disproportionately carries the burden of SCD due to vector prevalence and inadequate access to care.[3,15] While the overall SCD burden is expected to be greater in Africa and other malaria endemic regions due to malaria frequency, differences in access to economic and technological means for treatment has historically interfered with improvement of prevalence and manifestation globally.[1,3,20]

Sickle cell disease was not formally discovered in Western medicine until 1910, although tribes across Africa historically had many records of the disease.[7,21] Sixty-two years after the initial American discovery of SCD, the United States Congress passed the National Sickle Cell Anemia Control Act of 1972, the first federal attempt to educate America and create mass-screening programs across the country.[21,22] The first available treatments, such as blood

transfusions, gained popularity in 1984 and were followed by a series of new therapies like stem cell transplants, genotype modification, targeting of hemoglobin S polymerization, targeting vaso-occlusion, and targeting inflammation.[5,23] Privately insured SCD patients in the United States may spend up to $1.7M USD on direct medical costs associated with the disease before the age of 64,[24] even though the life expectancy of SCD patients in the USA is between 43 years to 55 years.[24,25] These incurred costs consist of the necessities such as comprehensive care for the duration of one's life including regular medical visits, prophylactic treatment, and any costs incurred during acute attacks. SCD, in itself, is taxing in both cost and physical effect. With the amount of money spent on care, attention should be called to cost reduction attempts and research for better methods and cures.

Disparities & Social Determinants of Health in the United States

Social determinants of health are defined as the environmental factors that play significant roles in defining the differences in health and quality-of-life for all groups of people.[14] These determinants are highlighted in the statistical difference in life expectancy at birth for non-Hispanic Black Americans, 70.8 years, versus the expectancy for non-Hispanic Whites, 76.4.[26] Additionally, Black Americans face higher percentages of comorbidities such as diabetes, hypertension, depression, solid cancers, among others and also experience more severe outcomes (*e.g.*, sickle cell crisis, hemochromatosis, stroke, and death) than white Americans.[13,15] These health disparities have been attributed to social differences between Whites and Blacks in the United States, such as decreased pediatric care, poor housing conditions, poor genetic health, and more.[7,27]

Understanding the biological and geographical implications of the existence of malaria in specific populations is important, however, social determinants of American healthcare ultimately create the specific disproportionalities discussed in relation to the virus and sickle cell disease. While social determinants can educate on who may be more susceptible to malaria infection and sickle cell disease naturally, the consequences of these natural inequalities are heightened by the formatted economic and racial systems that disproportionately effect those who suffer higher transmission rates and higher mortality rates than other populations.[7,26–28]

The racial gap in health, along with these social disparities, can be largely attributed to the systematic oppression of Black Americans throughout history, which contributed largely to the persistence of SCD over time. Stigmatization and prejudice based on race have become intertwined with SCD, leaving discrimination as the inferred reason for the delayed progress in sickle cell innovation. In the United States specifically, studies have shown that those with SCD have a long history of inadequate care, which has led patients to only visit doctors when their pain is excruciating due to distrust in care providers.[29–31] Those who have SCD also experience higher rates of substance abuse[29] and depression,[32] two conditions that may also severely affect physical health and general well-being. The disease itself is often falsely described as a "Black disease", a belief held by many Americans even though a wide range of races and ethnicities may have the disease.[33] This sentiment was even echoed by the then American President Richard Nixon, who stated "this disease is especially pernicious because it strikes only Blacks and no one else" in his statement when signing the National Sickle Cell Anemia Control Act of 1972.[34] Despite the fact that this act was meant to prevent stigmatization and discrimination based on SCD, this prejudice continued throughout the 1970s.[7] Modern prejudice is less explicit, but lack of cultural competency in academia and healthcare allows SCD to frequently and incorrectly be regarded as a disease of only Blacks or African Americans. Academia holds part of the blame, as only 9% (~189,000) of Bachelor's degrees awarded in a STEM field were to Black Americans in 2020,[35] even though Black and African Americans represented 12.4% (41.1 million) the country's population at the time.[36] Large groups of non-Black students completing STEM degrees may never meet a person suffering from SCD, and therefore never experiencing the severity of this problem first-hand. This, along with lack of funding, contributes largely to the lack of initiative for epidemiological research that could help improve the manifestation of SCD in the United States.[7,21] An ideal solution to improving cultural competency in rising healthcare workers is closing the race gap in graduating college students and prioritizing diversity and inequality initiatives in education. Though it may take many years to see the impact of a national educational intervention strategy such as this, the stated primary goals to reduce inequalities in SCD research and improve cultural competency should be pillars of academic and social advances.

Conclusion

With the negated benefit of protection from malaria, it is difficult to rationalize the perpetuated burden of sickle cell disease in Black Americans. Epidemiological patterns of disease prevalence in the United States demonstrate the undeniable relationship between these patterns and trends of biosocial isolation and health disparities.[3,13,37] It is by identifying and analyzing these influential factors that there is potential to reduce burden of the disease in America. Unfortunately, the translation of the growing knowledge about the disease translates very slowly into real solutions.[23,38] Many epidemiological researchers and specialists of health disparities are calling out this disproportionally slow innovation process, claiming it as another aspect of why SCD burden continues to be a prominent issue.[38] Without repairing systemic discrimination, we will always see disparities in the treatment of minority groups. In order to diminish the morbidity and mortality caused by SCD, equal research funding and continued widespread education present the best opportunities for continued improvement.

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