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Leukaemia burden in Africa

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Abstract

Leukaemia is cancer of the body's blood-forming tissues, including the bone marrow and the lymphatic system. Many types of leukemia exist. Some forms of leukemia are more common in children. Other forms of leukemia occur mostly in adults. Leukemia usually involves the white blood cells. Your white blood cells are potent infection fighters they normally grow and divide in an orderly way, as your body needs them. But in people with leukemia, the bone marrow produces an excessive amount of abnormal white blood cells, which don't function properly. Leukemia symptoms are depend on the type of leukemia. Common leukemia signs and symptoms include: Fever or chills, persistent fatigue, weakness, losing weight without trying, easy bleeding or bruising, swollen lymph nodes, enlarged liver or spleen, bone pain or tenderness. Diagnostic of leukemia in a routine blood test, before symptoms begin. If this happens, or if you have signs or symptoms that suggest leukemia, you may undergo physical exam, blood tests, and bone marrow test. Treatment for leukemia can be complex depending on the type of leukemia and other factors. Common treatments used to fight leukemia include: chemotherapy, targeted therapy, radiation therapy, bone marrow transplant and immunotherapy.

Keywords: leukaemia, Africa, burden, bone marrow, immunotherapy, radiation, chemotherapy,chronic myeloid leukaemia, acute myeloid leukaemia, lymphoblastic leukaemia

Introduction

Leukaemia is a blood-related malignancy characterized by transformed hematopoietic progenitors and diffuse infiltration of bone marrow (Wang *et al.*, 2019).The main types of leukaemia include acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML), chronic lymphocytic leukaemia (CLL), and chronic myeloid leukaemia (CML) (Suriyo *et al.*, 2019). Globally in 2020, leukaemia accounted for approximately 2.5% and 3.1% of all new cancer incidence and mortality, respectively. The risk of leukaemia varies among populations of different

ages, sexes, and geographical locations. Such disparities could be attributable to the difference in the prevalence of different environmental and genetic risk factors for leukaemia(Obeagu *et al.*, 2022; Obeagu *et al.*, Obeagu, 2022; Obeagu and Gnanavel, 2022; Obeagu and Obeagu, 2018; Obeagu and Babar, 2021).Risk factors for leukaemia include smoking, exposure to certain chemicals, chemotherapy in the past, radiation exposure, rare congenital diseases, certain blood disorders, family history, age, and gender. Due to the recent development of novel therapeutic strategies and targeted drugs, the overall survival of leukaemia patients has shown remarkable improvements. The epidemiology of leukaemia may have changed over time and may vary by different population groups. Therefore, it is imperative to examine the global disease distribution, risk factors, and trends of leukaemia to inform the development of its preventive strategies tailored for different countries(Obeagu, 2018; Obeagu, 2022; Obeagu *et al.*, 2022; Obeagu *et al.*, 2020; Obeagu and Obeagu and Obeagu, 2023; Obeagu *et al.*, 2022). Prior studies are limited to certain countries or captured temporal trends using relatively old data. Furthermore, none comprehensively determined the lifestyle and metabolic risk factors for leukaemia at a country level (Buffler *et al*., 2005).

Acute myeloid leukemia (AML)

Acute myeloid leukemia (AML) is a malignant disorder arising through the acquisition of genetic mutations in hematopoietic stem or progenitor cells, resulting in impairment of hematopoiesis and unrestrained proliferation of an immature clone. In the United States, the annual population incidence of AML in whites is 3.7 cases per 100 000 people, whereas in African Americans it is 2.9 cases per 100 000 people(Shaheen *et al*., 2021).

For a number of cancers, particularly cancers of the colon, breast, and prostate, whites have a more favorable prognosis than African Americans in the United States. The relationship between race and outcome is less clear in leukemia. African American children with acute lymphoblastic leukemia (ALL) are less likely to achieve remission and have an inferior disease-free and overall survival compared with white children with the same disease. One recent study from the Children's Cancer Group examined racial and ethnic differences in children with ALL and found that black children were overrepresented in high-risk characteristic groups and had a worse outcome compared with white children. Although data concerning incidence and outcome in AML according to race or ethnic group are sparse, Latinos appear to have a higher prevalence of one of the better-risk subtypes, acute promyelocytic leukemia (APL) (French-American-British [FAB] classification M3). It is unclear whether racial differences in subtypes and outcome in leukemia result from environmental or cultural influences, differences in genetics, or variability in reporting at diagnosis and/or follow-up (Shaheen *et al*., 2021).

Surveillance, Epidemiology, and End Result (SEER) Program data indicate that the age-adjusted mortality rate for AML is slightly higher in whites compared with African Americans (2.5 versus 2.0 per 100 000 US population). The age adjustment is important, as whites are diagnosed at a median of 67 years, while the median for African Americans is 60 years. It is not known whether AML-specific mortality differences between the 2 races exist nationwide. Additionally, race specific death rates do not control for other prognostic factors, including cytogenetics and AML subtype. Disparate cancer outcomes between races often are attributed to differential access to care, varying treatment aggressiveness and compliance, and biologic variability. Even if differential access to care and treatment aggressiveness are eliminated as potential confounders in describing racial differences in outcome for AML (as should occur within a cooperative group study), biologic variability may still play a role (Koolivand *et al*., 2018).

Chronic myeloid leukaemia

Chronic myeloid leukemia (CML) is a hematopoietic disorder characterized by the

malignant expansion of bone marrow stem cells. Its cytogenetic hallmark is a reciprocal t(9;22)(q34;q11) chromosomal translocation that creates a derivative $9q^+$ and a small 22q–, known as the Philadelphia (Ph) chromosome. The latter harbors the *BCR-ABL* fusion gene encoding a chimeric Bcr-Abl protein with a deregulated tyrosine kinase activity, the expression of which has been shown to be necessary and sufficient for the transformed phenotype of CML cells. CML is unusual among human cancers in that a single oncogene product has been identified as having a central role in its pathology (Minciacchi *et al*., 2021).

Chronic myeloid leukemia (CML) is a clonal hematopoietic stem cell disorder and accounts for approximately 30% of the incidence of adult leukemias. Life expectancy for patients with CML has substantially improved since the advent of tyrosine kinase inhibitors (TKIs) at the turn of the century. Of note, the prognosis of CML has changed from a fatal disease to a disorder that is compatible with a normal lifespan. As a result, the prevalence of CML has increased dramatically, and may reach a plateau in 2050s. However, the high-cost TKI treatment combined with the rising prevalence of CML has led to a high global burden of CML treatment. Therefore, comparable epidemiological statistics such as age-standardized rates (ASRs) are important metrics to assess the global burden of CML in different countries at various levels of economic development, which may show potentially distinct patterns that can direct health policy and health care resource allocation in the era of high-cost TKI therapy. Through the contribution of various researchers, the past 20 years have brought us considerable knowledge on the molecular and cell biology of CML, creating the essential platform for targeted therapy to be engineered. It soon became clear that the Bcr-Abl oncoprotein itself is the best molecular target presented by CML cells because it is not expressed by normal cells. Furthermore, the dissection of the signal transduction pathways affected by the deregulated kinase activity of Bcr-Abl provided information on additional or alternative signaling steps that could be interrupted in an attempt to eliminate the oncogenic effect of Bcr-Abl. More recently, attention has also been focused on immunological means of recognizing and destroying the leukemic clone, and these approaches look promising, particularly in the context of eliminating residual disease after various sorts of “debulking” therapy (García-Gutiérrez and Hernández-Boluda, 2019).
Until recently, CALL has been uncommon in sub-Saharan Africa, but there is now emerging a peak of incidence at the age 3 to 5 years in west and southern Africa. Prognosis for African patients with CALL is poor because of a multitude of clinical, biological and social factors. AML is seen at high frequency (probably indicating truly high incidence) in male children 5-14 years, of whom up to a quarter present with chloroma. It is predicted that the incidence of AML in adults may rise in the near future, related to cigarette smoking, occupational and environmental exposures to benzene and other pollutants, and the prescription of alkylating agents to young people with malignant disease. CML shows no particular epidemiological features, except for a high frequency in young adults and children, reflecting the age structure of the whole population. There are two forms of B-CLL: one is seen most commonly in women of low socioeconomic status towards the end of the their reproductive life, and is probably related to an initially polyclonal expansion of B-cells in response of recurrent malaria and other infections; the other is seen over the age of 45 years, with men being affected twice as commonly as women, as in the western world (Copland, 2021).

Acute Lymphoid Leukemia

Acute lymphoid leukemia (ALL) is a type of hematological neoplasm that affects the precursor cells of strains B, T and NK, with a higher incidence in the pediatric range. The pathophysiology of ALL is characterized by chromosomal abnormalities and genetic alterations involved in the differentiation and proliferation of lymphoid precursor cells. Despite the lack of information in the literature, it is believed that leukemogenesis originates from a complex interaction between environmental and genetic factors, which combined lead to cellular

modifications. Environmental factors have been evaluated as possible predisposing factors in the development of ALL but there are still conflicting results in the world literature. In this context, the aim of the present review is to discuss the major exogenous factors regarding ALL(Fujita *et al*., 2021).

Chronic lymphoid leukemia

The global incidence of leukemia has significantly increased over the years, with chronic lymphocytic leukemia (CLL) cases having a higher prevalence compared to all other lymphoid malignancies. Although the exact aetiology remains elusive, age, lifestyle and environmental factors have been identified as some of the major consequences implicated in the development of CLL. To date, it is well established that CLL is the most common type of leukemia, accounting for approximately 37% of all cases of blood malignancies, with an average global prevalence of about 3.5 cases per 100,000 people. In Africa, statistics on the incidence of CLL is very limited with isolated studies reporting on this form of leukemia. Nonetheless, various therapeutic drugs including those that modulate the function of immune checkpoints receptors are continuously being developed and their effectiveness tested in the management of patients with CLL worldwide (Abbas *et al*., 2015).

Immune checkpoints regulate immune function and play a crucial role in preventing autoimmunity. However, in CLL, the signaling of immune checkpoint receptors is dysregulated which results in immune dysfunction. Briefly, CLL is a monoclonal disorder that is characterized by the accumulation of functionally incompetent B-cells with a distinctive $CD19^{+}$, $CD20^{+}$, $CD5^{+}$, $CD23^{+}$ lymphocyte surface markers and surface immunoglobulin-positive phenotype in the peripheral blood, bone marrow, and lymph nodes. Hence, anti-CD20 monoclonal-based drugs such as rituximab and ofatumumab are used as standard treatment for CLL. However, these drugs are associated with severe adverse events such as neutropenia and thrombocytopenia, with others reporting on their ineffectiveness as monotherapy. Thus, the need to urgently broaden our understanding of the pathophysiological mechanisms implicated in the aggravation of CLL (Arruga *et al*., 2020) .

Although CLL is a B-cell malignancy, recent studies have also described the involvement of T-cells in the pathogenesis and progression of the disease. In fact in CLL, T-cell exhaustion mediated by an upregulation of coinhibitory receptors such as programmed death-1 (PD-1), lymphocyte-activation gene 3 (LAG-3), T-cell immunoglobulin-3 (TIM-3), and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) has been reported. Consequently, this has led to the advancement of immune checkpoint inhibitors that targets both B and T-cell function as a treatment strategy for CLL. However, contradictory findings on the effects of using immune checkpoint inhibitors in CLL patients have been reported. Thus, the exact effect of immune checkpoint inhibitors in CLL is contradictory and needs to be investigated further. As a result, due to high quality of evidence reported in randomized controlled trials (RCTs), this review will target such studies to assess and update available literature on the impact immune checkpoint inhibitors in CLL (Parikh *et al.*, 2020).

Conclusion

The differences in the incidence and clinical manifestations of leukaemias/lymphomas between the low-income regions of Africa and the high-income regions of the world are related to the differences in lifestyles that are prevalent in these varying parts of the world. They indicate the greater role of environmental pressures on leukaemogenesis compared to that of genetic differences of ethnicity and race. It is expected that as socio-economic differences among populations even out, so also will the observed differences in the epidemiological features of leukaemia/lymphoma.

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