

## Progress towards a cure for acute lymphoblastic leukaemia in Morocco

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Acute lymphoblastic leukaemia (ALL) is the most prevalent paediatric malignancy diagnosed worldwide, regardless of income (1). The cure rate is > 80% in developed countries because of effective and tolerable therapeutic protocols, and the most frequently used are the Group for Research on Adult Acute Lymphoblastic Leukemia protocols (2, 3). Successful treatment of ALL can be achieved by better understanding the biology of the disease, improved diagnostic methods, and implementation of an intensive risk-stratified treatment protocol, and intensive supportive therapy. It has been shown that accurate determination of risk status leads to cure in the majority of children with ALL after nonintensive treatment (4).

The situation varies geographically, with improved survival in low- and middle-income countries (LMICs) because of risk-adapted protocols, sophisticated risk stratification, and diagnostic techniques adapted to local contexts (1,5,6). In western countries, leukaemia incidence has been well established by many collaborative studies between professional societies and associations.

In Africa, particularly North Africa, we still have a long way to go to achieve good characterization of leukaemia. For example, despite the high frequency of T-cell acute lymphoblastic leukaemia (T-ALL), no structured studies have been carried out to date (7, 8). The absence of statistical data makes it impossible to monitor the epidemiology of this entity. In Morocco, the incidence and exact molecular characterization of T-ALL have not been established and are limited by lack of equipment, lack of access to appropriate facilities such as laboratories, and a lack of personnel trained in advanced molecular biological techniques. These limitations affect the diagnosis, prognostic stratification, and therapeutic strategy. The incidence of T-ALL was shown to be 31% in Morocco, which was similar to that in France (28.5%) and Italy (26.0%), higher than in the United States of America (20.0%), and lower than in Egypt (50%) and India (53.0%) (4,6,9–14). The cause of these disparities remains largely

unexplained, unless we consider low socioeconomic status as a key factor. Despite the presence of two national cancer registries in Casablanca and Rabat, the epidemiological profile of T-ALL is poorly understood in Morocco because of the absence of electronic medical records, and inaccurate and exhaustive collection and organization of incidence, prevalence, and survival data.

Since 2019, the Moroccan health ministry has considered management of paediatric cancer as a priority. In October 2019, Morocco was selected as a focus for implementation of the Global Initiative for Childhood Cancer. The results of the first investigation of survival rates for 6 WHO-indexed diseases in paediatric haematology and oncology units in Morocco have been published recently (15,16). The authors reported many obstacles to implementation of the Global Initiative for Childhood Cancer as well as a paediatric cancer plan. The lack of accurate data regarding the epidemiology and survival of childhood cancer was the first obstacle faced. Morocco, like many other LMICs, lacks functional data management systems. The results also highlighted priorities such as an urgent need to set up national cancer registries, including for paediatric cancer.

Treatment of ALL needs accurate diagnosis, risk stratification, adapted regimens for chemotherapy, and enhanced supportive care (17). The quality of care delivered to patients with ALL is closely linked to protocols that highlight diagnostic requirements, assess risk stratification, and indicate different types of drugs. Quality of care also depends on drug doses, anticipated duration of treatment, and supportive care. We suggest that protocols developed in high-income countries need coordinated adaptation to the local context of LMICs. All medical and nursing staff must be educated and monitored to adhere to proper implementation of newly adapted diagnostic and therapeutic procedures.

The documented incidence of childhood leukaemia is lower in LMICs than in more-developed countries. The geographic differences and different incidence

rates underline the importance of epidemiological investigations in LMICs, and implementation of hospital-based cancer registries as one of the next steps to improve cancer care. Complete and reliable registration of cancer cases needs prompt recognition of symptoms and early and correct diagnosis (14). In low-income countries where the performance of first-line health care is low, a non-negligible percentage of children with leukaemia may die before receiving diagnosis and registration. The lower survival rates in LMICs than high-income countries are largely because of inequity of diagnostic facilities and access to health care. Such barriers make timely access to accurate diagnosis complicated, and even when such diagnosis is possible, it may not be systematically reported in a cancer registry. Early and accurate diagnosis is the cornerstone of successful medical management. Unfortunately, low-income countries have few pathologists and centres to analyse samples and make a diagnosis (18). Many middle-income countries do not have access to adequate diagnostic capabilities, because of undertrained health workers or unavailability of pathological laboratories. As a result, the reported incidence of cancer can be lower than the actual rate.

How can we improve survival rates and patient outcomes even if our resources remain limited? A good starting point is to encourage and promote professional oncology partnerships between institutions in high-income and low- and middle-income countries to address

existing shortfalls, stimulate discussion between and within communities, assure accurate diagnosis, improve laboratory facilities, and define appropriate treatment plans (19). Correct diagnosis of leukaemia, which is a crucial first step in proper treatment and care, involves the combined efforts of many different specialists. The conventional laboratory tests for ALL include analysis of bone marrow cell morphology and cerebrospinal fluid. This diagnostic procedure should include immunophenotyping. Cytogenetic, and increasingly, molecular cytogenetic tests constitute important tools for disease classification but are not easily accessible at all institutions. WHO is aware of the situation and is trying to resolve the issues by engaging in the development of adapted approaches to the problems that focus on screening and early diagnosis. However, more needs to be done to identify biological differences among regions, which may require different therapeutic strategies, collaborative clinical trial development, improved access to drugs, and appropriate country-specific treatment guidelines.

The main message we want to convey is that we can make the vision of WHO a reality in LMICs by fostering collaboration between various partners and strengthening existing worldwide networks of partnerships, to enable leukaemia eradication through collaborative efforts.

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