

Mind the Gap: Improving Pediatric Cancer Care in Developing Countries

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ABSTRACT

Despite the fact that the majority of childhood cancer cases occur in the developing world, pediatric oncology in developing countries has not been afforded the ground breaking advances and successes that are available in developed countries. It is an underestimated global child health concern, and the factors contributing to the two-tiered cancer outcome profile between developed and developing countries are complex and expansive. There are some initiatives in place, such as the twinning program, that are successfully improving cancer treatment in resource-limited regions, but more international advocacy is needed to make state of the art cancer therapy available to all children.

RÉSUMÉ

Bien que la majorité des cas de cancers pédiatriques se produisent dans des pays en voie de développement, l'oncologie pédiatrique dans ces pays n'a pas pu profiter des avancées révolutionnaires qui sont accessibles dans les pays développés. Cela est un problème de santé pédiatrique mondiale sous-estimé, et les facteurs contribuant au profil à deux paliers des taux de survie du cancer entre les pays développés et ceux en voie de développement sont complexes et de grande ampleur. Il y a des initiatives en place, tels les programmes de jumelage, qui améliorent avec succès le traitement du cancer dans les régions possédant des ressources limitées, mais plus de défense internationale des droits des enfants est nécessaire pour assurer la disponibilité des toutes dernières thérapies contre le cancer pour tous les enfants.

INTRODUCTION

Pediatric cancer is often overlooked when discussing global child health due to the impact of infectious diseases on childhood mortality in developing countries. While infectious diseases are a child health concern, there is a decline in communicable diseases in developing countries while cancer causes a large and growing proportion of childhood mortality [1]. Almost 90% of the world's population of children live in low- and middle-income countries (LMIC) and this is where 84% of childhood cancers occur [2]. The wealth of cases in the developing world underlines the importance of developing strategies for improving pediatric oncology care in LMICs.

THE DISCREPANCY BETWEEN CANCER OUTCOMES IN HIGH-INCOME COUNTRIES (HICs) AND LMICs

A myriad of interrelated issues involving limited health care resources and poverty have shielded many of the recent advances made in cancer treatment and research from reaching developing countries. It is for this reason that they do not experience the positive outcomes found in high income countries (HICs), where over 80% of childhood cancers are cured [3].

One factor contributing to the poorer pediatric cancer outcomes in LMICs is that cancer is underdiagnosed and is often diagnosed at an advanced stage [4]. Embedded within this issue is the lack of population-based cancer registries in many developing

countries, thus limiting our knowledge of the extent of the severity of this problem. Retinoblastoma, a childhood cancer whose outcome largely depends on how early it is diagnosed, is a prime example of the disparities of disease outcomes between developing and developed countries. In developed countries, it is often diagnosed early and the disease-free survival probability reaches 80-90% [5]. Retinoblastoma unfortunately brews silently in LMICs and usually is not diagnosed until the metastatic stage, resulting in much lower survival rates. Some developing countries have implemented educational public awareness campaigns in an effort to diagnose retinoblastoma before it reaches the metastatic stage. A study conducted in Honduras provided positive results in support of the utility of educational campaigns [6]. After the initiation of a retinoblastoma education program to the public, adjoined with a vaccination clinic, the percentage of diagnosed cases showing extraocular spread decreased from 73% to 35% [6]. The educational program proved to be an effective and attainable method of combatting late diagnosis of the disease.

Leukemia is another childhood cancer that unfortunately has a worse outcome in LMICs compared to HICs (75% 5-year event free survival in HICs compared to 37% in LMICs) [7]. The poor outcome could also be attributed to the late diagnosis of this disease in developing countries. A study compared the time between initial symptoms and diagnosis in children with acute myeloid leukemia or acute lymphoblastic leukemia between two referral centres: one in Nicaragua and one in Italy [7]. It was

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shown that the median lag time was longer in Nicaragua than Italy (29 compared to 14 days) and this discrepancy was mainly due to 'physician delay,' which involved the timespan from initial consultation to diagnosis. The authors suggest that a medical educational program promoting suspicion for oncologic diseases for physicians could lessen the delay, as there was a shorter lag time in areas of Nicaragua with a childhood cancer training program in place.

Poor cancer outcomes in LMICs can also be partially explained by treatment abandonment, a major cause of therapeutic failure in the developing world. Treatment abandonment is defined as treatment that is initiated but not completed [8]. Of the new cancer cases that occur yearly in children aged 0-14, 15% were found to abandon treatment [9]. Although this study collected results from countries all over the world of different levels of income, 99% of cases of treatment abandonment were found to occur in LMICs. The reasons for abandonment of therapy in developing countries are numerous and vary greatly among countries and individuals. Many of these reasons are based upon limited financial and medical resources, and lack of social support [8]. For example, in Honduras a study showed that in a population of children with acute lymphoblastic leukemia, treatment abandonment was associated with travel time to the clinic and age younger than 4.5 years [10].

Malnutrition is also an important factor to consider in the discussion of negative outcomes in developing countries. In countries with limited resources, it is believed that malnutrition is present in 50% of children with cancer [11]. Nutritional status is tightly linked to therapeutic outcome as it can greatly affect the response to treatment, the development of comorbidities and the rate of overall survival [11]. There are gaps in knowledge in many areas concerning the particularities of these effects, therefore nutritional interventions should be further investigated to delineate some of these gaps [11]. In resource-limited LMICs, measuring nutritional status in children is another barrier as an inexpensive, accurate and widely available method must be used. There is also no current gold standard for measuring nutritional status, but techniques involving arm anthropometry are feasible in LMICs and have been shown to be more sensitive than those based on body weight [12]. Arm anthropometry measurements include mid upper arm circumference and triceps skin fold thickness, which determine lean body mass and fat mass, respectively [13]. It is important to recognize that there is a substantial void in normative data on body weight and composition of children in LMICs, which limits foundational knowledge for interventional studies.

A lack of supportive care resources in LMICs also plays a role in the poorer outcomes witnessed in the developing world. With a lack of resources in LMICs comes poorer infection control and

correspondingly higher rates of infection in neutropenic patients [4]. This underlines the importance of controlling nosocomial infections in LMICs. A lack of transfusion support is also detrimental to therapeutic outcomes in pediatric cancer. LMICs, which contain about 85% of the population, only collect half of the global blood donations [14]. Therefore, limited availability of blood products in these regions is a notable concern as many pediatric cancer patients may not have timely access to blood products when needed. Another crucial issue is the lack of palliative care in LMICs. With the large incidence of advanced stage cancer diagnosis in resource-limited countries, adequate palliative care programs are of utmost importance but are often lacking in oncologic units. A pediatric palliative care unit was developed in Pakistan in 2008 but there are problems still impeding its success, such as a lack of trained personnel, a lack of outreach programs, and insufficient morphine supplies [15].

TWINNING AND OTHER EDUCATIONAL INITIATIVES IMPROVE CANCER TREATMENT IN LMICs

In recent years, the medical community has become more cognizant of the disparities in pediatric cancer treatment in the developing world and several initiatives have been launched in an effort to improve outcomes in LMICs. An example of a prominent initiative that has proven to be effective is the twinning program. Devised as an effort to build pediatric oncology units in LMICs, the twinning program links an oncology unit in a developed country to a hospital in a developing country [16]. A successful example of the twinning program is the partnership existing between the Hospital for Sick Children in Toronto and Amman, Jordan [17]. This twinning program was a pioneer in the field of neuro-oncology in children – a type of cancer that is more difficult to treat due to the multidisciplinary nature of the specialists required for the appropriate care. The correspondence began with email communication and progressed to monthly video conferences and exchanges between the two institutions. Over the treatment period of the study, from 2002–2006, there was an overall 3-year survival rate of 100% in average risk patients and 81% in high-risk patients [17]. The researchers speculated that the twinning program aided the oncologists in Jordan to refine treatment protocols based on available resources, to develop the proper use of imaging techniques and to discuss exceptions in individual cases requiring special care. The collaboration allowed for valuable consultation between the two institutions and provided an educational experience on both ends.

Aside from the twinning program, more initiatives are in place to improve cancer care in LMICs. Some of these initiatives were designed to decrease the incidence of treatment abandonment, a primary reason for poor cancer outcomes in these regions. An example is a satellite clinic that was opened in Honduras to decrease the travel time to receive care [9]. The pediatric cancer

centre in Honduras is distant from population-dense regions so the implementation of this clinic should decrease travel time for 36% of patients and hopefully decrease the rate of treatment abandonment as well. Another effective initiative took place in Indonesia, where the implementation of a parental education program to poor families decreased the rate of treatment abandonment from 14% to 2% and increased the event free survival from 13% to 29% in poor patients [18]. These researchers were specifically concerned with education in poor families as treatment abandonment occurred at a much higher rate in poor patients, compared to prosperous ones.

FUTURE DIRECTIONS

Although there are many individual success stories in global pediatric oncology treatment, there is certainly more that can be done to ameliorate outcomes in developing countries. The formation of national child cancer strategies in these countries would be very beneficial as many countries have no overarching policy or structure for treatment [19]. A component of this national strategy should include the development of national standards of care and treatment protocols in LMICs. These standards should be developed according to available resources in the specific country and should be feasible to implement. The implementation of these standards should also include the development of risk stratification systems. Risk stratification systems are an integral part to standards of care as they allow for the optimization of treatment by matching the disease risk to treatment intensity to prevent over- or under-treatment. An example of a risk stratification system tailored to the resources available to the region was developed for neuroblastoma patients in developing countries [20]. A method of classifying disease risk based on clinical factors (age, serum ferritin, and serum lactate dehydrogenase) was shown to be just as effective as tests for genomic biomarkers and histological factors, and is more economically feasible in resource-limited areas.

The implementation of national cancer strategies would also involve mandatory reporting and registration of childhood cancer cases [19]. In 2006, only 21% of the world's population was covered in population-based cancer registries, with only 8% of the Asian population and 11% of the African population covered [21]. The collection of this data would allow researchers to determine the burden of disease in developing countries. They can then use this information to improve the efficiency of resource allocation, as well as determine the effectiveness of treatment policies [19].

CONCLUSION

With almost 90% of the world's population of children living in LMICs, pediatric cancer in these regions cannot be neglected [2]. There must be more advocacy on an international scale to work

to improve treatment efficiency and cure rates. Global initiatives by cancer centres in major academic institutions will provide the education and capacity to create sustainable programs to improve cancer care in developing countries. Striving for improvements in pediatric cancer outcomes in less developed regions of our world should be the next step in achieving breakthroughs in the management of this disease.

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