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A STUDY ON THE INCIDENCE AND MORTALITY OF LEUKEMIA AND THEIR ASSOCIATION WITH THE HUMAN DEVELOPMENT INDEX (HDI) WORLDWIDE IN 2012

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Abstract – *Objective:* *The present study was conducted with the aim to investigate the incidence and mortality of leukemia and their association with the Human Development Index (HDI) around the world in 2012.*

Materials and Methods: *This study was an ecologic study in the world to assess the correlation between Age-Standardized Incidence Rate (ASIR) and Age Standardized Mortality Rate (ASMR) of leukemia with HDI and its details that include: life expectancy at birth, Mean years of schooling and Gross National Income (GNI) per capita. ASIR and ASMR of leukemia expressed per 100,000 people. Statistical analyzes were performed using SPSS (Version 15.0, SPSS Inc., Chicago, IL, USA.)*

Results: *ASIR and ASMR of leukemia were 4.7 and 3.4 per 100,000 people, respectively. Countries with the highest ASIR were Mauritius (12), Cyprus (9.5), Canada (9.5), Ireland (9.4), and Australia (9.4). Also, countries with the highest ASMR were State of Palestine (7.7), Iraq (6.5), Mauritius (6), Syrian Arab Republic (5.7), and Ethiopia (5.4). There was a statistical significant and positive correlation between HDI and ASIR of leukemia ($r = 0.74$, $p \leq 0.001$), and HDI and ASMR of leukemia ($r = 0.369$, $p \leq 0.001$).*

Conclusions: *The highest incidence of leukemia occurred in countries with high and very high HDI and the highest mortality rate in countries with very high and moderate HDI. There was a significant positive correlation between ASIR and ASMR of leukemia with the HDI and its dimensions.*

KEYWORDS: *Incidence, Mortality, Leukemia, Human development index.*

INTRODUCTION

Cancer is one of the leading causes of mortality in developed and developing countries. It is expected that the incidence and burden of cancer will increase throughout the world due to the population growth and aging especially in less developed countries which account for about 82% of the world's population[1].

Leukemia is one of the most common cancers and the main cause of mortality from cancer in children[2,3]. It consists of a group of diseases characterized by malignant and uncontrolled proliferation of adult leukocytes or its precursors in the blood and bone marrow[4]. This disease is a heterogeneous group of cancers associated with the hematopoietic system and includes many different subgroups. Four main subgroups are diagnosed

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including Acute Lymphoblastic Leukemia (ALL), Acute Myeloid Leukemia (AML), Chronic Lymphocytic Leukemia (CLL), and Chronic Myeloid Leukemia (CML)[5-9].

In 2012, leukemia was reported as the 14th most common cancer and the 11th leading cause of mortality from cancer worldwide. This disease was ranked 10th in men and 11th in women in terms of incidence, and 8th in men and 9th in women in terms of mortality[1]. In general, this disease accounts for 2.5% of the total cancer cases and 2.3% of the total cancer mortality in people under the age of 75 years[10]. Despite the fact that leukemia is the most common malignancy among the people under the age of 20 years[11], most leukemia cases occur in the elderly, so that the highest incidence of this disease is observed in the age group of 65 and older. The Acute Lymphoblastic Leukemia (ALL) is the most common type of this disease in children, so that this type of illness accounts for 73% of all cases of leukemia in children, while the acute myeloid leukemia (AML) is the most common type of disease in people aged 20 to 40 years, and Chronic lymphocytic leukemia (CLL) and Chronic myeloid leukemia (CML) are more observed in the elderly[12].

Despite recent advances in understanding the pathophysiology of leukemia, the risk factors of this disease have not been fully and clearly diagnosed. However, some of the potential risk factors of this disease are obesity, overweight, smoking, exposure to benzene and high dose of ionizing radiation. These risk factors can be classified into several subgroups including the familial and genetic, lifestyle and environmental risk factors[13-16].

Unlike other types of cancer, leukemia is not a solid tumor that a physician can remove by surgery. In fact, the bone marrow is the source of this problem, thus its treatment is much more complex than other cancers[17]. The 5-year survival rate of Acute Lymphoblastic Leukemia (ALL) increased from 41% in the mid-1970s to 70% during 2004-2010, mostly due to the development of treatment protocols including the discovery of new therapies with better efficacy than previous treatments[18]. However, more than 50% of young people and 90% of the elderly die from leukemia in the first 5 years after diagnosis of disease. The resistance to primary treatment and relapse of diseases after complete recovery are the main barriers to treatment[19].

The socioeconomic status, educational level and life expectancy are among the reasons for difference in the incidence and mortality rates of cancers in different regions and they can be investigated using the Human Development Index (HDI). The HDI is a useful classification for comparing the incidence and mortality of cancers worldwide[20]. So far, the relationships of HDI and some cancers have been investigated. The investigation of these relationships can lead to a more accurate understanding of distribution of cancer and its risk factors worldwide[21,22]. Knowledge about the incidence and mortality rates of leukemia and its relationship with the HDI can be useful for health planning and research activities. The present study aimed to investigate the incidence and mortality of leukemia and their association with the HDI and its components in the world in 2012.

MATERIALS AND METHODS

This study was an ecologic study in the world to assess the correlation between Age-Standardized Incidence Rate (ASIR) and Age Standardized Mortality Rate (ASMR) of leukemia with Human Development Index (HDI) and its details that include: life expectancy at birth, mean years of schooling and gross national income (GNI) per capita. Data about the age-specific incidence and mortality rate (ASR) of countries for year 2012 get from global cancer project that available in (http://globocan.iarc.fr/Default.aspx)[10] and Human Development Index (HDI) from Human Development Report 2013[23] that include information about HDI and its details for every country in the word for year 2012. The method to estimate the age-specific incidence and mortality rates were published in the global cancer project by international agency for research on cancer[10,24].

In this study, we used the correlation bivariate method to assess the correlation between age-specific incidence and mortality rate (ASR) with Human Development Index (HDI) and its details that include: Life expectancy at birth, mean years of schooling and gross national income (GNI) per capita. Statistical significance was assumed if $p<0.05$. All reported *p*-values are two-sided. Statistical analyses were performed using SPSS (Version 15.0, SPSS Inc, Chicago, IL, USA).

RESULTS

Incidence of Leukemia

In 2012, there were 351965 cases of leukemia of which 200676 cases occurred in males and 151289 in females (Sex Ratio= 1.32). Among all cases, 130469 cases occurred in countries with very high HDI, 58981 cases in countries with high HDI, 136378 cases in countries with moderate HDI, and 26004 cases in countries with low HDI.

Five countries with the highest number of leukemia were China with 65778 cases, the United States with 39658 cases, India with 32532 cases, Russia with 11773 cases, and Germany with 11038 cases. Five countries with the highest number of leukemia in males were respectively China with 38394 cases, the United States with 22433 cases, India with 19619 cases, Germany with 6271 cases and Japan with 6046 cases. Five countries with the highest number of Leukemia in females were China with 27384 cases, the United States with 17225 cases, India with 12913 cases, Russia with 5903 cases, and Germany with 4767 cases.

The Age- Standardized Incidence Rates (ASIR) of Leukemia

The ASIR of leukemia per 100,000 people in the world was 4.7 (in men was 5.6 and in women was 3.9). The ASIR of leukemia was 7.2 in countries with very high HDI, 5.4 in countries with high HDI, 3.8 in countries with moderate HDI, and 2.5 in countries with low HDI. Five countries with the highest ASIR of leukemia were respectively Mauritius with a rate of 12, Cyprus with 9.5, Canada with 9.5, Ireland with 9.4, and Australia with 9.4. Five countries with the highest ASIR of Leukemia for males were Ireland with a rate of 12.5, Mauritius with 12.5, Australia with 11.7, Canada with 11.5, and Cyprus with 11.5. There were also five countries with the highest ASIR of Leukemia for females as follows: Mauritius with a rate of 11.5, Cyprus with 7.7, Canada with 7.6, Lithuania with 7.6, and New Zealand with 7.3.

Mortality of Leukemia

In 2012, there were 265471 deaths from leukemia of which 151231 cases occurred in males and 11450 cases in females worldwide (Sex Ratio=1.32). Among all cases, 84885 cases occurred in countries with very high HDI, 42847 cases in countries with high HDI, 113783 cases in countries with moderate HDI, and 23865 cases in countries with low HDI. Five countries with the highest number of mortality from Leukemia were China with 54719 cases, India with 2712 cases, The United States with 24729 cases, Japan with 8583 cases, and Indonesia with 8479 cases. Five countries with the highest number of mortality from leukemia in males were respectively China with 32596 cases, India with 16068 cases, the United States with 14154 cases, Japan with 5066 cases, and Indonesia with 4673 cases. Five countries with the highest number of mortality from leukemia in females were respectively China with 22123 cases, India with 10644 cases, the United States with 10575 cases, Indonesia with 3806 cases, and Russia with 3614 cases.

The Age- Standardized Mortality Rates(ASMR) of Leukemia

The ASMR of Leukemia per 100,000 people in the world was 3.4 (in men was 4.1 and in women was 2.8). The ASMR of Leukemia was 3.5 in countries with very high HDI, 3.8 in countries with high HDI, 3.2 in countries with moderate HDI, and 2.4 in countries with low HDI. Five countries with the highest ASMR of Leukemia were respectively State of Palestine with a rate of 7.7, Iraq with 6.5, Mauritius with 6, Syrian Arab Republic with 5.7, and Ethiopia with 5.4. Five countries with the highest ASMR of Leukemia for males were State of Palestine with a rate of 8.7, French Guiana with 7.6, Iraq with 7.6, Syrian Arab Republic with 6.9, and Yemen with 6.9. There were also five countries with the highest ASMR of Leukemia for females as follows: State of Palestine with a rate of 6.7, Iraq with 5.8, Mauritius with 5.4, Timor-Leste with 5.4, and Ethiopia with 5.1.

The Relationship Between ASIR of Leukemia and HDI

There was a statistical significant and positive correlation equal to 0.74 (p<0.001) between the ASIR of Leukemia and the HDI. Furthermore, there was a positive correlation between components of the HDI and the ASIR of Leukemia, so that there was a positive correlation of 0.726 ($p \leq 0.001$) between the ASIR and life expectancy at birth, and with average education years equal to 0.672 ($p \leq 0.001$), and with the income level per person in the population equal to 0.507 ($p \leq 0.001$) (Figure 1).

The Relationship Between ASMR of Leukemia and HDI

There was a statistical significant and positive correlation equal to 0.369 ($p \leq 0.001$) between ASMR of Leukemia and HDI. Furthermore, there was a positive correlation between components of HDI and ASMR of Leukemia, so that there was a positive correlation of 0.471 ($p \leq 0.001$) between the ASMR and life expectancy at birth, and with average education years equal to 0.313 ($p \leq 0.001$), and with the income level per person in the population equal to 0.133 ($p \leq 0.001$) (Figure 2).

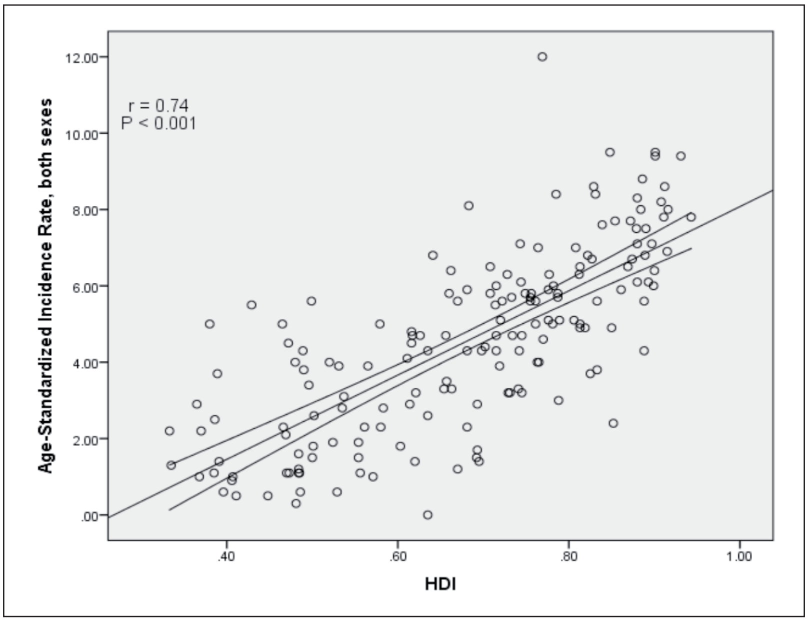

Fig. 1. Correlation between Human Development Index (HDI) and ASIR of leukemia in the world in 2012.

DISCUSSION

In general, 351965 new cases and 265471 deaths from leukemia were recorded in the world in 2012, and the sex ratio (male to female) was 1.32 for incidence and mortality of leukemia. This difference may be due to the differences in the anti-oxidative capacity, sex chromosomes, gene expression, hormones, behavior, the availability and use of healthcare and differences in the environmental exposure such as higher prevalence of alcohol consumption and smoking in men than women[25-30]. Therefore, leukemia occurs in both genders and all age groups, but this disease is the most common childhood cancer and accounts for about 30% of whole cancer in the age group of less than 15 years[31-33].

In the present study, countries with the highest ASIR of leukemia were put in the rank of countries with high HDI in terms of development index, and those with the highest mortality from leukemia were put in the rank of countries with moderate and very high HDI. The results of a study in the United States also indicated that the incidence of some cancers including leukemia was increased in both men and women over the period of 2007-2011[33], as chronic lymphocytic leukemia was the most common type of leukemia

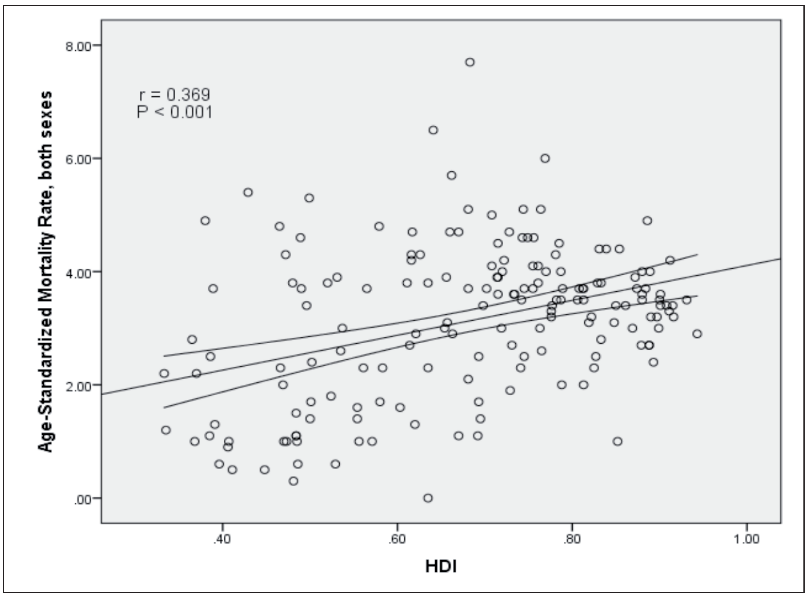

Fig. 2. Correlation between Human Development Index (HDI) and ASMR for Leukemia in the world in 2012.

in adults in the Western countries; and about 30% of all leukemia cases were related to this type of disease. In contrast, this type of leukemia is rare in Asia and includes less than 5% of all cases[34]. The air pollution is a possible risk factor for leukemia especially in developed countries. According to the conducted study in Canada, one of the chemical compounds of air pollution called nitrogen dioxide (NO_2) is associated with leukemia[35]. Studies in Michigan and China[36,37] also showed that an increased risk of mortality from leukemia was associated with exposure to benzene. Other risk factors for leukemia were smoking, overweight and obesity which were more prevalent in developed countries and were associated with increased incidence and mortality of leukemia and all of its types in adults, especially in men. It is also likely that the increased risk of leukemia in obese people is due to other behavioral factors associated with the obesity[4,38].

Life expectancy at birth is a dimension of the HDI and has a positive and significant correlation with ASIR of leukemia. Other investigations also showed a positive correlation between the ASIR of cancer and life expectancy at birth, so that the highest incidence of cancer was related to Europe, and it had the highest life expectancy (76.8 years) among multiple regions of WHO, but the lowest incidence rate for all cancers was seen in Africa with the lowest life expectancy (60 years)[39]. Therefore, the cancer is a disease associated with age, and despite the fact that leukemia is the most common malignancy in children, most cases of leukemia occur in the elderly[12].

In the present study, there was a positive correlation between the life expectancy at birth and the ASMR from leukemia. In general, survival rates were reduced with increasing of age and life expectancy, especially for AML, which was the most common type of leukemia in adults[40, 41]. The mortality from the ALL, CLL and CML also increased with age[42], because the effect of treatment was lower on older people, and they could not tolerate aggressive therapies and their conditions that might be a serious threat to their lives[43]. Physicians might also be less likely to treat older people with aggressive therapies[44].

In the present study, there was a positive and significant correlation between the ASIR and ASMR of leukemia with the average years of education in the societies. However, some studies reported a negative correlation between the level of education and the incidence and mortality of leukemia. The level of education was related to exposure to important risk factors of cancer such as smoking and obesity[45]. The results of a study in the United States also indicated that an increase in the educational level was associated with a decrease in the prevalence of cigarette smoking, and this could lead to a reduction in the incidence of cancer in people with higher education levels. The mortality rate from cancer was also significantly affected by the educational level[45]. The educational level might be related to behavior, health conditions or access to knowledge and resources that had direct and indirect impact on the survival of the cancer[46-50]. The results of another study also showed that the rate of cancer survival was greater in people with higher education than those with low education[50].

In this study, there was a positive and significant correlation between the ASIR of leukemia and income level Gross Domestic Product per Capita (GDP), as another component of the HDI. Similar results were observed in other researches[51]. However, other studies found that the family income had an inverse relationship with the risk of childhood leukemia[52]. It seemed that the direction of the relationship was largely dependent on design of study, place, time and difference in the evaluation of socioeconomic status (SES) level methods[53-55].

In this study, there was a positive and significant correlation between the ASMR of leukemia and income level (GDP). Evidence suggests that the income has an inverse relationship with leukemia deaths, since in societies with a higher socio-economic level, early detection can improve the patients' survival[50]. For example, a study in Sweden showed that in this country, like many other developed countries, individuals with higher social and economic levels suffer from lower rates of chronic illness, which will ultimately lead to greater success in treating and improving the survival of cancer in these patients[56,57].

CONCLUSIONS

The highest incidence of leukemia occurred in countries with very high and high HDI. The highest mortality rate occurred in countries with very high and moderate HDI. There was a significant relationship between ASIR and ASMR of leukemia with the HDI and its dimensions. Therefore, it is necessary to investigate the causes of this cancer in order to reduce the incidence and mortality of leukemia, especially in areas with high incidence and mortality.

Conflict of Interest:

The Authors declare that they have no conflict of interests.

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