# DISABILITY-ADJUSTED LIFE YEARS OF LEUKEMIA CANCER IN CHILDREN 0-14 YEAR IN ASIA FROM 2010 TO 2019: A SYSTEMATIC ANALYSIS FOR THE GLOBAL BURDEN OF DISEASE STUDY 2019

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**ABSTRACT** – **Objective:** Childhood leukemia is the most frequent form of cancer in children. Despite the fact that most children diagnosed with leukemia are cured, many of them experience long-term complications.

**Materials and Methods:** An ecological study was conducted utilizing data related to healthy life years lost due to disability (YLDs), years of life lost due to premature death (YLLs), and disability-adjusted life years (DALYs) caused by leukemia cancer (chronic and acute) in children from the Global Burden of Disease (GBD). We used correlation tests at the 0.05 level to examine the correlation between these indicators and the human development index.

**Results:** The highest DALYs and YLLs in 2010 and 2019 were associated with Low Socio-Demographic Index (SDI) regions, while the highest number of YLDs in 2010 and 2019 were related to High-middle SDI regions in the continent. In Asia, the burden of disease, YLDs and premature death were higher in men than in women from 2010 to 2019. Our results demonstrated a negative and significant correlation between DALY (r=-0.563, $p$=0.0001) and YLL (r=-0.571, $p$=0.0001) with the human development index in Asian countries. However, the correlation between the index of YLD (r=- 0.108, $p$=0.483) and the human development index was not significant.

**Conclusions:** To reduce the risks associated with leukemia cancer, policymakers should take the necessary measures to improve healthcare systems, promote early diagnosis and treatment, and provide health education to reduce exposure to risk factors related to leukemia cancer. Countries with low human development index have a higher burden of leukemia, which indicates the need for targeted interventions to lower the burden of childhood leukemia in these regions.

**KEYWORDS:** Leukemia cancer, Children, Burden of disease, Asia, HDI.

## INTRODUCTION

Leukemia is a hematologic malignancy marked by abnormal stem cell proliferation and loss of hematopoietic tissue function[1]. Leukemia's etiology is still unknown, but risk factors such as age, medical history, environmental conditions, and genetic mutations have been identified to affect clinical outcomes[2,3].

Childhood leukemia represents the most commonly diagnosed malignancy in this population. About 80% of childhood leukemia diagnoses are caused by Acute Lymphoblastic Leukemia (ALL), while about 15-20% are caused by Acute Myeloid Leukemia (AML). ALL and AML have significant differences in epidemiological patterns based on age, ethnicity, and gender[4] . Additionally, molecular characteristics and leukemogenic susceptibility associated with specific exposures distinguish childhood from adult forms of these diseases[5].

The incidence rate of ALL is 42 cases per million children, with a peak incidence in early childhood between ages 1 and 4 being nearly 100 cases per million. Incidence rates are higher in men compared to women up to the age of 19[6].

There is a significant variation in incidence across the globe due to the heterogeneity of childhood leukemias. According to GLOBOCAN 2018 estimates, leukemia was the 15th most commonly diagnosed cancer and the 11th leading cause of cancer death globally, accounting for 437033 cancer cases and 309006 cancer deaths. Mortality and incidence rates were higher in men than women. In 2018, the age-standardized incidence rate for men and women was different, with men having an incidence rate of 6.1 compared to 4.3 per 100,000 for women. In addition, mortality rates for men were higher (4.2 per 100000) than those observed for women (2.8 per 100000)[7].

In developing countries, there are 1 to 40 new cases per million people[8,9]. From 2005 to 2015, the total number of leukemia cases increased by 26%, but population growth and aging were only responsible for 3% of this increase[10]. All-cause cancer survivors face the risk of long-term cognitive impairment, obesity, chronic debilitating conditions, congestive heart failure, second neoplasms, and premature mortality[7].

The Human Development Index (HDI) is commonly used to assess a country's development based on health, education, and standard of living dimensions[11,12]. Several studies have explored the incidence and mortality rates of leukemia across different countries and regions and their relationship with HDI in low- to medium-HDI nations[13-16] . Therefore, this study aims to investigate the relationship between childhood leukemia burden (chronic and acute) and HDI in Asian countries.

## MATERIALS AND METHODS

This study presents a correlation analysis examining the relationship between health indices and human development indices. Data pertaining to disease burden index, YLL (Years of Life Lost), and YLD (Years Lived with Disability) were retrieved from the Global Burden of Disease website (http://ghdx. healthdata.org/gbd-results-tool). The Disability-Adjusted Life Year (DALY) health index was utilized to calculate the years of life lost either due to premature death or non-fatal diseases that result in disability. This index was developed by the Global Burden of Diseases and Injuries (GBD) study to assess the overall burden of diseases. Meanwhile, the HDI is a composite measure of average achievement across key dimensions of human development, including long and healthy life, education, and standard of living. This measure is calculated as the geometric mean of normalized indices for each dimension, where the health component is determined by life expectancy at birth, the education component is estimated based on average years of schooling among adults aged 25 and above and expected years of schooling for school-age children, while the standard of living component is measured by gross national income per capita[16,17].

### Statistical Analysis

Bivariate correlations were computed to analyze the data, with the significance level set at $p>0.05$. Stata software version 12 was employed for the statistical analyses (Stata Corp., College Station, TX, USA).

## RESULTS

The results showed that in 2010, the highest DALY [DALY=216.46, (154.06, 311.55)] was observed in Africa, while the highest YLD [YLD=3.84(2.58, 5.42)] occurred in Asia, and the highest YLL [YLL=213.5(151.71, 306.94)] was also recorded in Africa. Similarly, in 2019, the highest DALY [DALY=171.07, (124.85, 222.790)] was observed in Africa, while the highest YLD [YLD=3.24(2.23, 4.5)] occurred in Europe, and the highest YLL [YLL=168.75, (123.14, 219.260)] was recorded in Africa (Table 1).

**Table 1.** Comparing DALY, YLL and YLD rate per 100000 of leukemia cancer (chronic and acute) in children 0-14 year by continent (source: Global Burden of Disease 2019).

| Region | 2010 | | | 2019 | | |
|---|---|---|---|---|---|---|
| | DALY | YLD | YLL | DALY | YLD | YLL |
| America | 191.51 (174.96, 209.18) | 2.78 (1.96, 3.75) | 188.72 (172.48, 206.49) | 156.73 (134.8, 181.25) | 2.3 (1.57, 3.23) | 154.43 (132.84, 178.84) |
| Africa | 216.46 (154.06, 311.55) | 2.96 (1.61, 4.55) | 213.5 (151.71, 306.94) | 171.07 (124.85, 222.79) | 2.32 (1.36, 3.43) | 168.75 (123.14, 219.62) |
| Asia | 181.75 (148.8, 219.86) | 3.84 (2.58, 5.42) | 177.91 (145.25, 215.34) | 143.03 (123.49, 167.82) | 3.23 (2.2, 4.5) | 139.8 (120.52, 164.26) |
| Europe | 113.45 (102.06, 123.11) | 3.74 (2.59, 5.03) | 109.71 (98.55, 119.04) | 87.49 (77.47, 98.5) | 3.24 (2.23, 4.5) | 84.24 (74.68, 94.76) |

Figure 1 presents an analysis of the global burden of leukemia cancer in children from 2010 to 2019 by continent and gender, indicating a negative trend globally. This suggests a decrease in the burden of leukemia cancer in children worldwide in 2019 compared to 2010 (Figure 1).
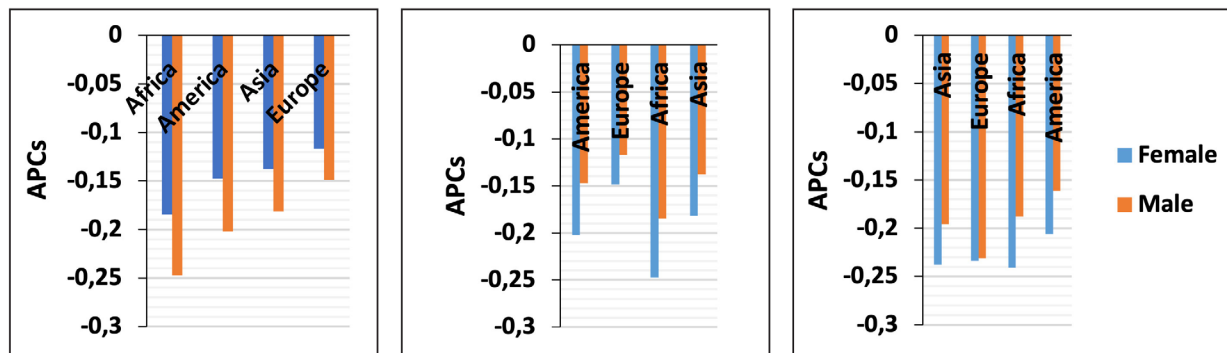


**Figure 1.** Annual percentage changes (APCs) of leukemia cancer (chronic and acute) in children 0-14 year of 2010-2019 by continent (source: Global Burden of Disease 2019).

Similarly, Figure 2 shows the trend in the burden of disease in the Asian continent during the same period, where men had a higher burden of disease, YLD, and YLL. However, the burden of leukemia cancer has decreased in both genders over time in this region.
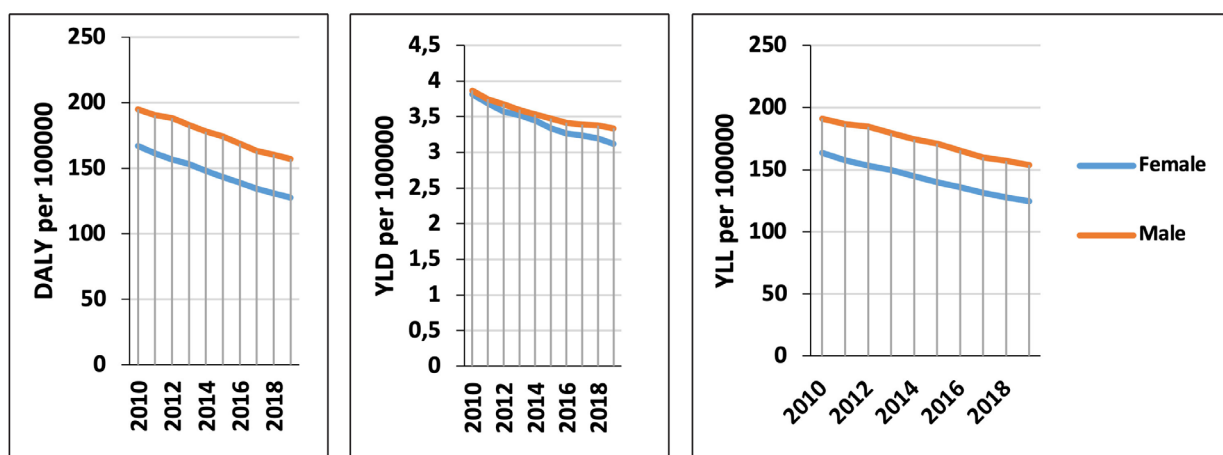


**Figure 2.** Trend DALY, YLL and YLD rate leukemia cancer (chronic and acute) in children 0-14 year of 2010-2019 in Asia by sex (source: Global Burden of Disease 2019).

Table 2 illustrates that low Social Development Index (SDI) areas had the highest DALYs and YLDs in 2010 and 2019. Furthermore, the highest YLD in both years analyzed corresponded to high-middle SDI areas.

**Table 2.** DALY, YLL and YLD rate per 100000 of leukemia cancer (chronic and acute) in children 0-14 year by SDI (source: Global Burden of Disease 2019).

| | DALY | | YLL | | YLD | |
|---|---|---|---|---|---|---|
| | **2010** | **2019** | **2010** | **2019** | **2010** | **2019** |
| **Low-middle SDI** | 171.64 (127.29, 221.19) | 135.67 (111.23, 165.1) | 169.15 (125.41, 217.98) | 133.73 (109.12, 162.6) | 2.49 (1.44, 3.82) | 1.94 (1.26, 2.77) |
| **Low SDI** | 243.85 (168.02, 366.75) | 197.4 (145.55, 261.27) | 240.62 (165.67, 361.2) | 194.79 (143.81, 256.84) | 3.23 (1.64, 5.16) | 2.61 (1.5, 3.9) |
| **High SDI** | 69.41 (65.38, 72.6) | 59.6 (54.84, 64.8) | 66.4 (62.7, 69.26) | 56.81 (52.46, 61.53) | 3.00 (2.08, 4.07) | 2.78 (1.94, 3.88) |
| **Middle SDI** | 199.86 (179.67, 229.97) | 151.86 (128.71, 175.78) | 195.64 (175.78, 222.53) | 148.47 (125.88, 171.91) | 4.22 (2.93, 5.88) | 3.38 (2.31, 4.86) |
| **High-middle SDI** | 169.91 (150.84, 184.03) | 130.65 (109.39, 150.63) | 165.12 (147.12, 178.59) | 126.35 (106.12, 145.42) | 4.79 (3.28, 6.53) | 4.3 (2.85, 6.13) |

**Supplementary Table 1** compares the status of leukemia cancer burden in 2010 *vs.* 2019 based on Asian countries, with Azerbaijan having the highest rates of DALYs and premature deaths due to leukemia cancer in both years analyzed. The highest rate of YLD and YLL due to leukemia in children was also observed in Azerbaijan in 2010 and 2019.

Our analysis found that a substantial and adverse correlation exists between DALY (r=-0.563, $p$=0.0001) and YLL (r=-0.571, $p$=0.0001) with respect to the HDI in Asian nations. However, no significant correlation was observed between HDI and the index of YLD (r=-0.108, $p$=0.483) (Figure 3).
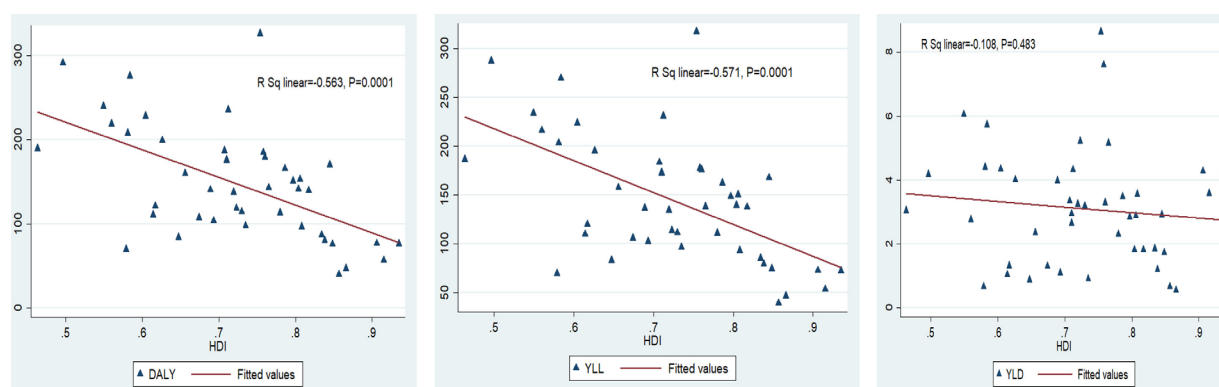


**Figure 3.** Correlation between the HDI, DALY, YLL and YLD rate of leukemia cancer (chronic and acute) in children 0-14 in Asia 2019.

The results of the analysis of variance indicate that the highest DALY (240.193 per 100000), the highest YLL (235.77 per 100000), and the highest YLD were observed in regions characterized by low HDIs, whereas the corresponding figures were found to be lower in areas with very high HDI, and this difference was statistically significant (Table 3).

**Table 3.** Relationship level human development to DALY, LYY and YLD rate per 100000.

| | DALY, LYY and YLD rate per 100000 | | |
|---|---|---|---|
| | DALY | YLL | YLD |
| **Very high Human development** | 95.484 | 93.103 | 2.375 |
| **High Human development** | 166.921 | 162.978 | 3.939 |
| **Medium Human development** | 155.841 | 153.233 | 2.603 |
| **Low Human development** | 240.193 | 235.77 | 4.423 |
| **P(F-test)** | *p<0.001* | *p<0.001* | *p<0.05* |

## DISCUSSION

From 2013 to 2017, leukemia and lymphoma accounted for 39.0% of all cancers in children and adolescents under the age of 20. The incidence of leukemia in this age group was reported to be 4.7 per 100,000. Although most children with leukemia are now cured, many suffer from long-term complications. A report by the GBD 2017 Childhood Cancer Collaborators showed that leukemia accounts for the largest proportion of childhood cancer DALY burden worldwide, with an attributable deficit of 34.1% (34.0–34.1). Among all subtypes, acute lymphoblastic leukemia (ALL) accounted for the highest proportion[18]. The early onset of leukemia indicates that exposure to risk factors before and after birth plays a crucial role in the development of leukemia in childhood, especially ALL[19]. Our study revealed a decrease in the burden of leukemia in Asia in recent years, which may be attributed to advancements in treatments associated with them and decrease in the incidence , as well as environmental factors such as smoking cessation, increased folate and vitamin supplement consumption during pregnancy, and extensive genetic screening for high-risk component mutations[20-23].

Overall, according to the findings, the global burden has decreased with negative annual percent change values, likely because of higher living standards and advances in medical technology[24,25]. Establishing better medical systems for leukemia diagnosis and information acquisition25 is crucial for developing regions and countries[25]. Our study also found that burden of leukemia is higher in men than women, in line with previous studies demonstrating greater disease prevalence in men[26-29]. According to the American Cancer Society's 2019 report, 55% of new cases and 56% of all deaths occurred in men[30]. Men have a higher exposure to leukemia risk factors, including lifestyle and occupational factors (smoking, ionizing/non-ionizing radiation, hydrocarbons, and pesticides)[31-33]. In addition, our study showed that DALY (r=-0.563, *p*=0.0001) and YLL (r=-0.571, *p*=0.0001) have a significant negative correlation with the HDI in Asian countries. Research has demonstrated that the burden of leukemia is associated with the HDI and gross domestic product (GDP) per capita. It may be difficult for Lower-income countries to provide adequate medical care and access to drugs to patients, which may necessitate the use of additional resources to reduce the disparity in survival[25]. Our variance analysis revealed that Low HDI was related to the highest rate of DALY (240.193 per 100,000), highest rate of YLL (235.77 per 100000), and highest rate of YLD. Leukemia deaths and DALYs have been attributed to occupational exposure to benzene and formaldehyde, with sensitivity to these carcinogens higher in more deprived areas, possibly contributing to high incidence rates, deaths, and DALYs in children living in such regions[34-37]. In order to reduce exposure to associated risk factors and address the future burden of leukemia, it is important for policymakers to prioritize improved medical systems, early diagnosis and treatment, and health education. While the 2019 GBD study provided updated data, certain limitations were inevitable due to limited diagnostic accuracy, misreporting, and misdiagnosis. Such limitations are improving over time. The 2019 GBD study provides us with updated data, however, based on some objective conditions, so several limitations will be unavoidable, due to the limitation of diagnostic accuracy, misreporting and misdiagnosis may cause deviations in the actual number of cases, especially in some underdeveloped countries.

## CONCLUSIONS

In this study, it was shown that the burden of leukemia cancer in children is decreasing in recent years and there are noticeable changes between DALY in the countries of the region. We also found that the burden of leukemia is higher in men and that the burden of disease is lower in regions with higher HDI, so it is imperative for policymakers to further improve health care systems, strive for early diagnosis and treatment, educate and promote hygiene to reduce people's exposure to associated risk factors.

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