

Incidence and pattern of leukemia in Bhutanese population: a retrospective analysis of eight years (January 2008 to December 2015)

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ABSTRACT

Introduction: The burden of haematological malignancies in developing countries is on the rise. This burden may be further aggravated in Bhutan due to the aging population and rapid modernization of the nation. Despite this, there is a paucity of information about the incidence and pattern of leukemia in the Bhutanese population. In this retrospective study, we aim to investigate the incidence and pattern of leukemia in Bhutan using a database of leukemia diagnosed at Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan from January 2008 to December 2015. **Methods:** The diagnoses and classification of leukemias were based on the morphology of blood cells on peripheral blood and bone marrow smears. The data was analyzed with descriptive statistics. The age-standardized incidence rate per 100,000 populations and its 95% confidence interval was calculated to assess the statistical significance. **Results:** In total 118 patients were diagnosed with leukemia over the period of eight years. Leukemia was found to be more frequent in male (51.69%) compared to female (48.30%) with a male to female ratio of 1.1:1. Acute leukemia accounted for 66.95% of all leukemia case diagnosed, whereas chronic leukemia accounted for only 33.05% of the cases. The average, annual, age-standardized incidence rate of leukemia per 100,000 population was 2.30 (95% CI: 1.87-2.73). **Conclusions:** The incidence and pattern of leukemia in the Bhutanese population is similar to other published literature. Leukemia is not uncommon in the Bhutanese population, thus additional studies on risk factors for leukemia in the Bhutanese population is necessary.

Keywords: Bhutan; Haematological malignancy; Incidence and type of leukemia.

INTRODUCTION

There is an increasing trend in the global burden of cancer due to aging and growth of the world population. The burden is further aggravated by the adoption of cancer causing behaviours, particularly smoking in economically developing countries¹. The International Agency for Research on Cancer (IARC) estimated 14.1 million new cancer cases in 2012 worldwide, of which 8 million occurred in economically developing countries. In 2012, cancer caused about 2.9 million and 5.3 million deaths in economically developed and developing countries respectively². A haematological malignancy was responsible for about 6.5% of all cancers worldwide in 2012, and it is predicted to increase by about 48% in developing countries by 2030 as compared to 2012. The prevalence of these malignancies is higher in western countries; however, these incidences are rapidly increasing in developing countries whereas the increasing trend is not observed in developed countries³. Leukemia is a haematological malignancy resulting from the neoplastic proliferation of haemopoietic or lymphoid cells⁴.

Leukemia is broadly divided into chronic and acute leukemia. Acute leukemia's are a heterogeneous group of neoplasms arising from transformation of uncommitted or partially committed haematopoietic stem cells⁵. The acute leukemia's are further divided into Acute Myeloid Leukemia (AML) and Acute Lymphoid Leukemia (ALL) based on the lineage involved. According to the French American British classification (FAB), AML consists of eight subtypes (M0-M7) and ALL consist of three subtypes (L1-L3). Chronic leukemia includes Chronic Myeloid Leukemia (CML) and Chronic Lymphoid Leukemia (CLL). CML is a clonal stem cell disorder characterized by increased proliferation of myeloid elements at all stage of differentiation. CLL is characterized by the accumulation of non-proliferating mature appearing lymphocytes in the blood, marrow, lymph nodes, and spleen⁵. For the past few decades, Bhutan has experienced rapid modernization. With this new era, peoples are exposed to various carcinogenic substances, thus like other malignancies we may see a rise in the number of leukemia cases as the nation develops. Additionally, the number of elderly persons in Bhutan (60 years and above) is expected to increase drastically from 29,745 (4.7 %) in 2005 to 111,000 persons (11.2 %) in 2045⁶. This drastic rise in the geriatric population may also increase the burden of cancer in Bhutan. Leukemia is frequently encountered in our routine practice; however, there is no published data regarding the incidence and pattern of leukemia in

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the Bhutanese population. In this retrospective study, for the first time we report the incidence and pattern of leukemia in Bhutan.

METHODS

In this retrospective cohort study, all the leukemia cases diagnosed from January 2008 to December 2015 at the Haematology Unit, Department of Pathology and Laboratory Medicine, Jigme Dorji Wangchuck National Referral Hospital (JDWRH) were included as study sample. The study was carried out over the period of one month (01-02-16 to 30-02-16).

All the leukemia cases were diagnosed based on the morphology of blood cells on peripheral blood and bone marrow smears. All the data of leukemia cases (year, diagnosis, age, and sex) that are documented by the haematology unit were compiled and individually checked for duplication. The refined data was analyzed with use of descriptive statistics. The age-standardized incidence rate per 100,000 population was calculated using the world standard population. Ninety five percent confidence interval was calculated for age-standardized incidence rate to assess the statistical significance. The study protocol was reviewed and approved by the Research Ethics Board of Health, Ministry of Health, Bhutan via letter no: REBH/Approval/2015/046.

RESULTS

Out of 118 patients, 51.69% ($n=61$) were male and 48.30% ($n=57$) were female. The sex ratio (male/female) was 1.1:1. The youngest leukemia patient was a 13 day old female who suffered from AML secondary to Down Syndrome, on the other hand, the oldest was an 89 year old female who suffered from AML. Acute leukemia accounted for 66.95% ($n=79$) of all leukemia cases diagnosed, whereas chronic leukemia accounted for only 33.05% ($n=39$) of the cases. Within acute leukemia, 51.89% ($n=41$) of the patients suffered from AML and 48.10% ($n=38$) from ALL. In chronic leukemia, 82.05% ($n=32$) of the patients were suffering from CML and 17.95% ($n=7$) from CLL. For AML, 53.66% ($n=22$) of cases were observed in females and 46.34% ($n=19$) in males. The ALL cases were equally distributed between males and females. In chronic myeloid leukemia, there is a higher frequency for males (59.38%, $n=19$) compared to females (40.63%, $n=13$); similarly, the frequency of CLL for males (57.14%, $n=4$) was higher than females (42.86%, $n=3$). The median age for leukemia patients in years were 39.93, 25.63, 38.55 and 52.71 years for AML, ALL, CML and CLL respectively. Acute leukemia's were observed in all ages; however, the frequency of AML was highest in middle age adults and ALL was highest in young adults (Figure 1). CLL

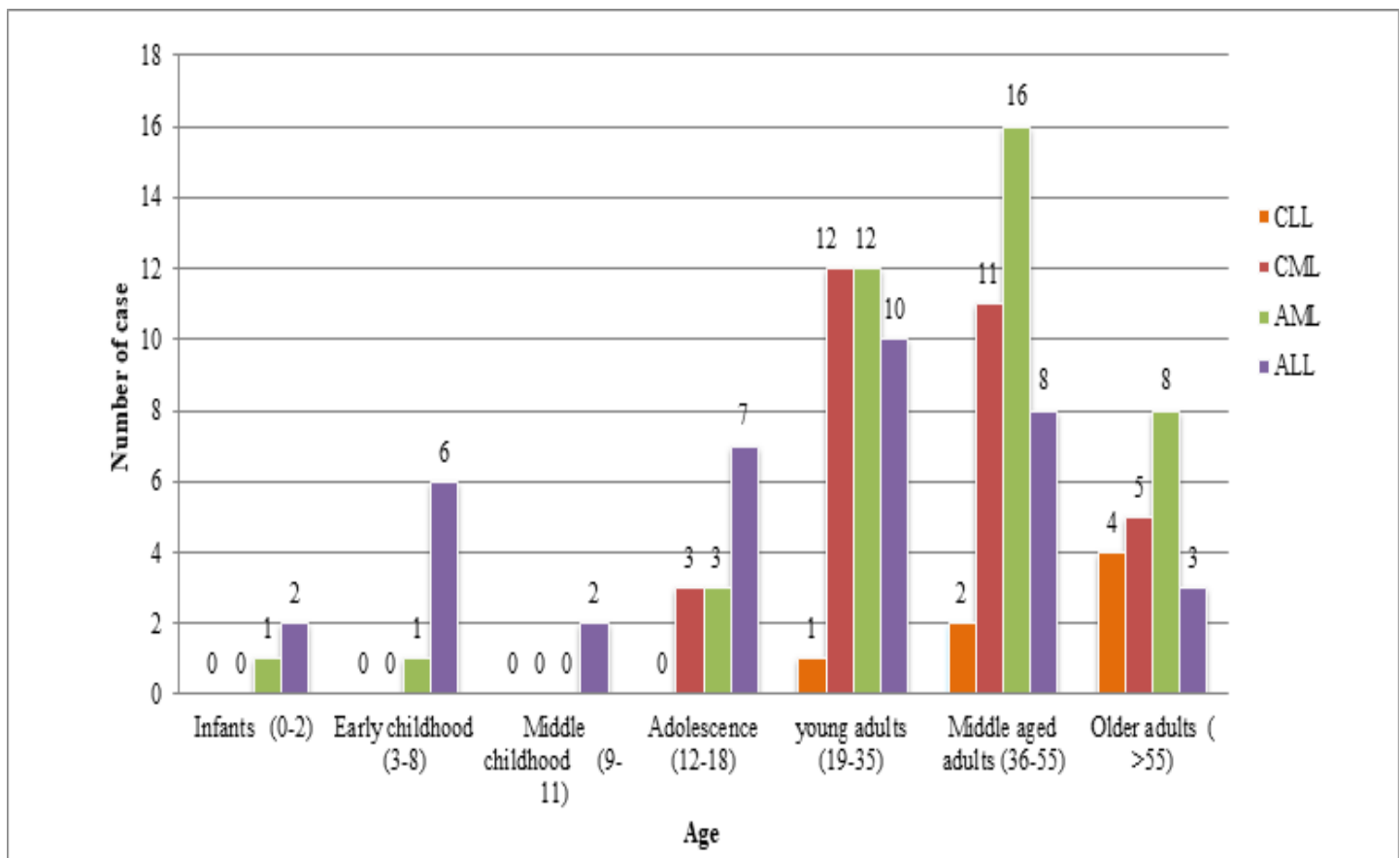


Figure 1. Distribution of various leukemia in different age group

Table 1. Number of leukemia cases observed and crude estimated number of patients expected per year

Leukemia type	Number of case	Distribution (%)	Medianage (Year)	Age range (years)	Average number of patients expected per year
CLL	7.00	5.93	52.71	28-65	0.88
CML	32.00	27.12	38.55	17-72	4.00
AML	41.00	34.75	39.93	13 days-89	5.13
ALL	38.00	32.20	25.63	2- 72	4.75
Total	118.00	100.0			14.76

was observed only in adults with increasing frequency with age. Similarly, most of the CML cases were observed in adults with few cases in adolescence. The average, annual, age-standardized incidence rate (ASR) of leukemia per 100, 000 population was 2.30 (95% CI: 1.87-2.73). The average leukemia cases expected per year was 14.76 (Table 1).

DISCUSSION

To our knowledge, this is the first exhaustive study regarding the incidence and pattern of leukemia in the Bhutanese population. The average, annual, age-standardized incidence rate (ASR) of leukemia per 100, 000 population was 2.30. This finding was comparable with the age-standardized incidence rate of 3.0 leukemia cases per 100,000 population in Saudi Arabia reported by International Agency for Research on Cancer (IARC) in 2008⁷. However, the incidence of leukemia was found to be higher in Northwest Iran⁸. In this study, the frequency of leukemia was found to be higher for males, a similar higher frequency in males was also reported from Bangladesh, Iran and India^{3,8,9}. Furthermore, Bangladesh reported the highest frequency in males compared to India. Acute leukemia was found to be the predominant leukemia in the Bhutanese population. This predominance of acute leukemia was also reported in other studies^{3,10}. Interestingly, CLL was found to be commonest leukemia in both sexes in Ireland¹¹. A study on prevalence of leukemia in North West Frontier Province of Pakistan reported that AML was only slightly higher than ALL and it was also found more frequent in adults¹², which was also observed in our study. The frequency of CML in our study was 27.12%, which is higher compared to the other published literatures from the region³; however, the median age of 38.55 years at the time of diagnosis was comparable. CLL is the least encountered leukemia in most populations outside the United States and Europe¹³. In our study, the incidence of CLL was only 5.93% and this supports the paucity of CLL outside the United States and Europe. Although, less compared to the other leukemias, higher incidences of CLL (10% and 19.7%) compared to our findings were reported^{9,14}. The median age for CLL patients

at the time of diagnosis was 52.7 years, supporting the higher incidence of CLL in adults. Similar findings of median age at the time of diagnosis were also published⁹; however, high median age of 72 years at the time of diagnosis has also been reported¹⁵.

CONCLUSIONS

The overall findings of incidence and pattern of leukemia in Bhutanese population is comparable with other published literature. Our study revealed that leukemia is not uncommon in the Bhutanese population. Considering the qualitative and quantitative inadequacy of haematological services in Bhutan, the finding of an incidence rate of 2.30 cases per 100,000 population may represent the tip of an iceberg. Furthermore, the rapid development of the nation and the aging population may increase this incidence. Hence, further investigation of risk factors for leukemia in Bhutan is necessary.

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AUTHORS CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

KD: Concept, design, literature search, data collection and analysis, manuscript writing and review.

RJ: Concept, design, data analysis, manuscript writing and review.

PDS: Concept, design, data analysis, manuscript writing and review.

PR: Concept, design, data analysis, manuscript writing and review.

DW: Concept, design, data analysis, manuscript writing and review.

Author agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

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