The burden of leukemia in the Kingdom of Saudi Arabia: 15 years period (1999–2013)

Amen Bawazir1,5*, Nouf Al-Zamel2, Abeer Amen3, Maaged A. Akiel4,5, Naif M. Alhawiti4,5 and Ali Alshehri1

Abstract

Background: Leukemia is a malignant neoplasm that arises from hematopoietic cells. The number of leukemia cases has dramatically increased from 297,000 to 437,033 cases worldwide. As result, the Saudi Cancer Registry ranked leukemia as the 5th type of cancer cases among both genders in Saudi Arabia. Data on the trend and incidence of leukemia in Saudi Arabia is lacking. This study aims to report the trend and incidence of leukemia in Saudi Arabia using available data from the Saudi Cancer Registry (SCR), as a population-based cancer registry in the country over a period of 15 years (1999–2013).

Methods: Data of registered leukemia cases between years 1999–2013 were retrieved from the Saudi Council of Health, Saudi Cancer Registry. Data were coded using the International Classification of Diseases for Oncology (ICD-O). Main and essential variables were retrieved such as age, sex, years of incidence, residency, and histopathological type of leukemia.

Results: A total of 8712 cases of leukemia were analyzed in this study, 57.2% were males and 42.8% were females. Around 33.6% of cases were from the central region of Saudi Arabia. The most diagnosed type of leukemia was the Precursor B-cell lymphoblastic leukemia (18.7%), followed by Precursor cell lymphoblastic leukemia, NOS (17.3%) with equal percentage of reported cases between males and females in these subsets.

Conclusion: Over a period of 15 years, the trend of leukemia showed the likelihood of increase in rate particularly in males with highest incidence reported from the central region of Saudi Arabia which needs more investigation. Resources for diagnosis and treatment should be planned with more orientation toward the accurate diagnosis of leukemia to minimize the number of “none specific diagnosis”.

Keywords: Leukemia, Incidence, Cancer, Burden, Saudi Arabia

Background

Leukemia is a malignant neoplasm of hematopoietic origin, characterized by diffuse replacement of bone marrow and peripheral blood with neoplastic cells [1]. Although, many subtypes of leukemia were known, four main subtypes were frequently seen in diagnosis such as: Acute Myeloid Leukemia (AML), Chronic Myeloid Leukemia (CML), Acute Lymphoblastic Leukemia (ALL) and Chronic Lymphocytic Leukemia (CLL). Globally, between 1990 to 2018, the number of leukemia cases markedly increased from 297,000 to 437,033 [2]. Thus, according to GLOBOCAN report in 2018, leukemia was ranked the 13th among cancers worldwide, while leukemia deaths increased by 16.5% in the same year. Despite the increased incidence of leukemia over the time, causes of leukemia are still not clear. Both genetic and environmental risk factors such as exposure to ionizing radiation, infection, or chemical substances contribute heavily to the development of leukemia [3]. Consequently, such wide range of risk factors affects prognosis, treatment plans and overall survival [4].

According to the reported data from the GLOBOCAN for region of Middle-East and Northern Africa (MENA), the estimated crude incidence is 5.3 per 100,000 among male population and 4.0 per 100,000 females [5]. Moreover, Gulf Cooperation Council report on cancer, ranked...
leukemia as the 4th among the most common cancers in the area [6].

The national healthy survey reported that increased prevalence of leukemia lesions among Saudi population is alarming for the healthcare service. This is because of serious complications of leukemia. In 2017, the Saudi Cancer Registry, stated that leukemia was ranked 5th among cancers in both genders of all ages in the Saudi population. The overall prevalence of leukemia was 7.6% in males and 4.4% in females in Saudi population [7]. When looking at the age group of older than 14 years of age, leukemia ranked in the top seventh (3.7%), while it ranked the first (38.8%) among Saudi children of less than 14 years of age, with higher rates in males compared to females (59.6% vs. 40.9%).

In this study, we aim to define the burden patterns and trends of leukemia over the period 1999–2013 within Saudi population using the SCR. In addition, the study is aimed to identify the most common types of leukemia in different ages, genders, and regions in the Saudi population. This descriptive study would provide helpful information to decision makers to better understand the demographics of leukemia in Saudi Arabia to help identify patients groups with highest burden to the healthcare system.

Methods

Study design and setting

A retrospective descriptive epidemiological analysis of all Saudi leukemia cases was retrieved from the SCR between January 1st, 1999 and 31st of December 2013 (15 years period). Saudi Arabia is a vast country extending over four-fifths of the Arabian Peninsula. It is approximately 2,149,700 km² in area. According to the national estimation in the year 2015, Saudi citizens were around 19,863,975 with dominant of young population as seen in the population pyramid (Fig. 1) [8].

Saudi Cancer Registry is a population-based registry of all cancer cases registered since the year 1992. The registry is housed in the Department of National Registries in the Saudi Health Council under the admiration of Saudi Ministry of Health (MOH). The SCR strives for full access to cancer data from all Ministry of Health and other governmental and private hospitals, as well as clinics and laboratories throughout the following administrative areas of the country: Riyadh, Qassim, Hail, Dammam, Al Ahsa, Hafr Al-Batin, Jeddah, Makkah, Taif, Qunfudhah, Abha, Asir, Baha, Najran, Jazan, Bisha, Madinah, Tabuk, Jouf and Northern regions of the Kingdom. Thus, the SCR covers all regions of Saudi Arabia as mentioned above. Cancer data are abstracted from patients’ medical records, based on clinical and/or histopathological diagnosis, by SCR certified tumor registrar [9]. A ministerial decree has categorized cancer as a mandatory notifiable disease. This ensures the opportunity for comprehensive data collection from all over the stated regions and health care services. Although the registry reported Non-Saudi cancer cases, this work is reporting only for Saudi nationality.

Study subjects and data collection

Inclusion criteria

All Saudi patients recorded in the registry with diagnosis of leukemia, both genders, in different age groups between the periods of 1st January 1999 to 31st December 2013 were included in this study.

Exclusion criteria

Non-Saudi patients with leukemia and registered cases missing principle data, such as age, topography, or sex

Fig. 1 Population pyramids of Saudis (%) by gender and age group, 2015. Male  Female
Identification were excluded in this study (11 cases (0.126%).

Requested data from the SCR were serial number, gender, age, address, nationality. Moreover, data related to tumor details like diagnosis date, primary site, histology, behavior, grade, stage, basis of diagnosis and status of the patients (death, alive) were also collected. The primary site (topography) and histology (morphology) of the malignancies are identified and coded according to the International Classification of Diseases for Oncology 3rd Edition (ICD-O-3), published by the World Health Organization (WHO), 2000, while those reported initially with ICD-O-3 codes are converted to ICD-10 for analysis purposes [10, 11].

Statistical analysis
Data were received from the SCR in a flash disc in form of Excel Sheet and arranged in column based on the required variables as mentioned above. Data were reviewed for incompleteness or missing entries and then entered into the computer package using IBM SPSS Software (Statistical Package for the Social Sciences, version 20, Chicago, Ill, USA). Continuous variables such as age were summarized and reported with mean and standard deviation (±SD). Categorical variables such as gender, types of leukemia included Precursor B-cell lymphoblastic leukemia, Precursor cell lymphoblastic leukemia, NOS, Chronic myeloid leukemia, NOS, Acute myeloid leukemia, NOS, B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma, Precursor T-cell lymphoblastic leukemia, Acute promyelocytic leukemia, t(15;17)(q22;q11–12), Acute monocytic leukemia, Acute leukemia, NOS, Acute myelomonocytic leukemia, Acute myeloid leukemia with maturation, Acute myeloid leukemia without maturation, Chronic myelogenous leukemia, BCR/ABL positive were categorized” and presented in frequency and percentages. A two-sided chi-square test was used for independence categorical data with a P-value of (<0.05) considered significant in this study. Estimation of the population based on sex was obtained annually from the Annual Year Book from the General Authority of Statistics/kingdom of Saudi Arabia [12]. The incidence rate was calculated based on midtime of the total population denominators in the country for the period 1999–2013. The World Standard Population was also used for direct standardization to calculate age-standardized rates per 100,000 populations. The age category classification of the IARC was used, [5] based on age groups of five-year interval (0–4 up to 70–74) patients older than 75 were noted as ≥75. Moreover, the Age-standardized rate is a summary measure of a rate that a population would have if it had a standard age structure. The World Standard Population was used to calculate this stage. The calculated incidence is known as the World Standardized Incidence Rate and the rate is expressed per 100,000 populations.

Ethics approval and consent to participate
No need for informed consent because the used data was aggregation of secondary data. However, all the data retrieved from the SCR were anonyms just with coded number and without any link to patient’s identity. The proposal of this study was approved by the research committee in the College of Public Health and Health Informatics at the King Saud Bin Abdulaziz University for Health Sciences (KSAU-HS) and thenafter reviewed and approval by the research committee in the King Abdullah International Medical Research Centre (KAIMRC) in the ministry of National Guard Health Affair, Riyadh, Kingdom of Saudi Arabia under the reference (SP 17/030/IR).

Results
Sociodemographic characteristics
A total of 8,712 leukemia cases were documented in the SCR during the study period 1999–2013. The mean age was 30.4 (±SD 25.6), 4,984 (57.2%) males and 3,728 (42.8%) were females. The Central region reported the highest rates (33.6%) among other Saudi administrative regions, while Madinah region reported the lowest (14.3%) (Table 1).

Five years age-adjusted incidence rate (ASR) by gender of Saudi leukemia cases (1999–2013) was analyzed. In general, the overall ASR was 5.3/100,000 population, however, males showed higher incidence than females (5.9 vs. 4.6 per 100,000 population). According to age groups, the overall highest ASR of leukemia was reported in the youngest age group of 0–4 years old (1.0/100,000 population), followed descendently by each age group, while the lowest ASR was seen in the middle-age group of 25–39 years old (2.0/100,000 population). Similar trend was found when comparing leukemia ASR by gender (Table 2).

| Table 1 Sociodemographic characteristics of the study population (1999–2013) |
|-----------------------------|--------|--------|
| Variables                        | No.  | %     |
| Mean age (±standard deviation)   | 30.4 (±25.6) |        |
| Gender                        |        |        |
| Male                        | 4,984 | 57.2  |
| Female                    | 3,728 | 42.8  |
| Regions                     |        |        |
| Central               | 2,908 | 33.6  |
| Western            | 1,860 | 21.5  |
| Eastern          | 1,407 | 16.2  |
| Southern       | 1,254 | 14.5  |
| Madinah      | 1,238 | 14.3  |
| Total                      | 8,712 | 100   |
When analyzed the trend of leukemia over the period of 15 years in Saudi Arabia, it shows a steady increase with higher rate of recently reported cases since the year 1999 up to 2013 (5.2 and 7.9%) with similarity in both genders, however the observed differences, was not statistically significant. Leukemia trend was also varied among different administrative regions, with highest rates in children (younger than 5 years of age) among cases reported from Central region of Saudi Arabia (34.2%), followed by adults (15–59 years), and then elder age groups (more than 60 years of age) with 33.1, and 33.3%, respectively, but did not showed statistical significant differences (Table 3).

Analysis of age groups of leukemia cases by gender showed no significant differences between the genders in children and adult age groups, however among the elder groups significant differences was found between genders ($p < 0.001$), but not between regions (Table 4).

Types of leukemia by gender
According to the morphology classified of leukemia cases, 15 types of leukemia were enumerated in this study. The highest reported type was Precursor B-cell lymphoblastic leukemia (18.7%) with equal percentage in both males and females, followed by precursor cell lymphoblastic leukemia not specify [(NOS) (17.3%)], and then chronic myeloid leukemia, NOS (13.0%). The lowest reported type was acute myeloid leukemia without maturation and chronic myelogenous leukemia, BCR/ABL positive (1.2% for each). Chi-square test showed strong significant differences between males and females according to type of leukemia ($p$-value < 0.001) (Table 5).

Trend of leukemia in Saudi Arabia overtime
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Distribution of leukemia subtypes by region

Significant differences and variation in the rate of leukemia were found between the subtypes of leukemia and regions of the kingdom ($p < 0.01$). While the Central region had the highest number of precursor B-cell lymphoblastic leukemia cases (21.8%), the western region showed the highest rate in precursor cell lymphoblastic leukemia NOS (21.5%). Also, precursor cell lymphoblastic leukemia, NOS had the highest number in Madinah region (19.1%), followed by precursor B-cell lymphoblastic leukemia (18.3%). The lowest reported subtypes were chronic myelogenous leukemia, BCR/ABL positive (0.6%) in the southern region and also leukemia, NOS (0.7%) in the Central region of the country. In Eastern region the acute myeloid leukemia was reported with higher rate in comparison to other regions (13.1%) (Table 6).

Diagnostic and prognostic characteristics of leukemia among Saudi regions (1999–2013)

A total of 8712 cases of leukemia in all Saudi regions were diagnosed by blood and bone marrow examinations, followed by other types of diagnostic methods ($p < 0.01$). According to the Immunophenotyping diagnostic procedure, the B-cell leukemia was highest in all the regions (84.3%), followed by T-cell (14.7%). Rates of cancer related deaths were so close to the overall causes of death in the study population, which ranged from 27.1% in the Western region to 30.0% in the Central region of Saudi Arabia (Table 7).

Incidence of leukemia

The overall incidence of leukemia during the period (1999–2013) has steadily increased among both genders (Fig. 2). However, it is more in males than females. In 2012, the peak among males was reported in the as 5.5 per 100,000 person per year in 2013, while in females it was reported as 4.3 per 100,000 person per year in the year 2011, as shown in Fig. 2. This increase in 2012 was

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Table 5 Leukemia subtypes by gender (1999–2013)*

| Variables                                      | Male          | Female         | Total          |
|------------------------------------------------|---------------|----------------|----------------|
| Morphology                                     | No. | %   | No. | %   | No. | %   |
| Precursor B-cell lymphoblastic leukemia         | 934 | 18.7| 696 | 18.7| 1,630| 18.7|
| Precursor cell lymphoblastic leukemia, NOS     | 875 | 17.6| 630 | 16.9| 1,505| 17.3|
| Chronic myeloid leukemia, NOS                  | 575 | 11.5| 556 | 14.9| 1,131| 13.0|
| Acute myeloid leukemia, NOS                    | 554 | 11.1| 486 | 13.0| 1,040| 11.9|
| B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma | 499 | 10.0| 251 | 6.7 | 750 | 8.6 |
| Precursor T-cell lymphoblastic leukemia        | 256 | 5.1 | 67  | 1.8 | 323  | 3.7 |
| Acute promyelocytic leukemia, t(15;17)(q22;q11–12) | 155 | 3.1 | 160 | 4.3 | 315  | 3.6 |
| Acute monocytic leukemia                       | 125 | 2.5 | 109 | 2.9 | 234  | 2.7 |
| Leukemia, NOS                                  | 129 | 2.6 | 89  | 2.4 | 218  | 2.5 |
| Acute leukemia, NOS                            | 99  | 2.0 | 99  | 2.7 | 198  | 2.3 |
| Acute myelomonicytic leukemia                  | 94  | 1.9 | 105 | 2.8 | 199  | 2.3 |
| Acute myeloid leukemia with maturation         | 83  | 1.7 | 83  | 2.2 | 166  | 1.9 |
| Acute myeloid leukemia without maturation      | 50  | 1.0 | 53  | 1.4 | 103  | 1.2 |
| Chronic myelogenous leukemia, BCR/ABL positive | 59  | 1.2 | 48  | 1.3 | 107  | 1.2 |
| All others                                     | 497 | 10.0| 296 | 7.9 | 793  | 9.1 |

*p value of < 0.001
also observed in young males of less than 14 years of age, Fig. 3. The peak of incidence in young males was 4.0 per 100,000 people per year, while it was 3.0 for young females. In adults of more than 14 years of age, both males and females showed an incidence of 2.7 per 100,000 populations per year (year 1999), while females dropped to 1.8 per 100,000 per year in 2013 (Fig. 4). The overall incidence during the period (2001–2013) among the elderly age group (more than 60 years of age-76). Both genders showed a steadily increased of leukemia with more trend in males than females, Fig. 5. For example, the peak was reported as the highest among male cases in the year 2006 (21.2 per 100,000 person-year), while highest incidence rate was found in the year 2006 in females (14.3 per 100,000 person-year) (Fig. 5).

**Discussion**

Leukemia is considered as an important public health problem in Saudi Arabia for it is impact in causing deaths among young people. In this country, around one fourth of the population are children less than 14 years old, highlighting the huge burden of such malignant blood disease. Therefore, the reported mean age in this study was 30.4 years from the total included patients in

| Table 6 The distribution of leukemia subtypes among the regions (1999–2013)* |
|---------------------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Regions                  | Central No. | Central % | Eastern No. | Eastern % | Madinah No. | Madinah % | Southern No. | Southern % | Western No. | Western % | P value |
| Precursor B-cell lymphoblastic leukemia | 635 | 21.8 | 237 | 16.8 | 226 | 18.3 | 238 | 19.0 | 288 | 15.5 | 0.297 |
| Precursor cell lymphoblastic leukemia, NOS | 409 | 14.1 | 240 | 17.1 | 237 | 19.1 | 215 | 17.1 | 400 | 21.5 | |
| Chronic myeloid leukemia, NOS | 375 | 12.9 | 177 | 12.6 | 152 | 12.3 | 173 | 13.8 | 251 | 13.5 | |
| Acute myeloid leukemia, NOS | 334 | 11.5 | 184 | 13.1 | 145 | 11.7 | 160 | 12.8 | 204 | 11.0 | |
| B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma | 275 | 9.5 | 111 | 7.9 | 89 | 7.2 | 113 | 9.0 | 155 | 8.3 | |
| Precursor T-cell lymphoblastic leukemia | 129 | 4.4 | 38 | 2.7 | 34 | 2.7 | 39 | 3.1 | 82 | 4.4 | |
| Acute leukemia, NOS | 25 | 0.9 | 20 | 1.4 | 14 | 3.7 | 13 | 4.3 | 62 | 3.3 | |
| Acute monoblastic leukemia | 98 | 3.4 | 46 | 3.3 | 21 | 1.7 | 24 | 1.9 | 44 | 2.4 | |
| Acute promyelocytic leukemia, t(15;17)(q22;q11–12) | 114 | 3.9 | 63 | 4.5 | 40 | 3.2 | 48 | 3.8 | 50 | 2.7 | |
| Leukemia, NOS | 20 | 0.7 | 45 | 3.2 | 81 | 6.0 | 25 | 2.0 | 45 | 2.4 | |
| Acute myelomonocytic leukemia | 74 | 2.5 | 30 | 2.1 | 26 | 2.1 | 27 | 2.2 | 42 | 2.3 | |
| Acute myeloid leukemia with maturation | 72 | 2.5 | 24 | 1.7 | 21 | 1.7 | 20 | 1.6 | 29 | 1.6 | |
| Chronic myelogenous leukemia, BCR/ABL positive | 31 | 1.1 | 19 | 1.4 | 9 | 0.7 | 8 | 0.6 | 40 | 2.2 | |
| Acute myeloid leukemia without maturation | 42 | 1.4 | 15 | 1.1 | 16 | 1.3 | 14 | 1.1 | 16 | 0.9 | |
| All others | 275 | 9.5 | 158 | 11.2 | 95 | 7.7 | 107 | 8.5 | 152 | 8.2 | |

*p value of < 0.001

| Table 7 Diagnostic and prognostic characteristics of leukemia cases among Saudi regions (1999–2013) |
|-----------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Regions                    | Central No. | Central % | Madinah No. | Madinah % | Southern No. | Southern % | Western No. | Western % | P value |
| Immunophenotyping          |                   |                   |                   |                   |                   |                   |                   |                   |                   |
| B-cell                     | 1,050 | 83.7 | 487 | 84.4 | 411 | 88.2 | 419 | 84.8 | 572 | 82.5 | 3,008 | 84.3 | 0.297 |
| T-cell                     | 206 | 15.6 | 85 | 14.7 | 53 | 11.4 | 67 | 13.6 | 110 | 15.9 | 523 | 14.7 | |
| Grade I -IV                | 4 | 0.3 | 2 | 0.3 | 1 | 0.2 | 2 | 0.4 | 2 | 0.3 | 12 | 0.3 | |
| Killer cell                | 2 | 0.2 | 1 | 0.2 | 1 | 0.2 | 1 | 0.2 | 2 | 0.3 | 7 | 0.2 | |
| Null cell                  | 3 | 0.2 | 2 | 0.3 | 0 | 0.0 | 5 | 1.0 | 7 | 1.0 | 17 | 0.5 | |
| Basis of Diagnosis         |                   |                   |                   |                   |                   |                   |                   |                   |                   |
| Histology of primary       | 2,080 | 71.8 | 1,006 | 72.5 | 704 | 58.4 | 815 | 65.4 | 1,172 | 63.5 | 5,805 | 67.3 | 0.001 |
| Death Certificate Only     | 36 | 1.2 | 30 | 2.2 | 74 | 6.1 | 38 | 3.0 | 47 | 2.5 | 228 | 2.6 | |
| Others                     | 780 | 26.9 | 351 | 25.3 | 427 | 35.4 | 394 | 31.6 | 628 | 34.0 | 2,594 | 30.1 | |
| Causes of Death            |                   |                   |                   |                   |                   |                   |                   |                   |                   |
| Cancer                     | 873 | 30.0 | 372 | 26.4 | 359 | 29.0 | 355 | 28.3 | 504 | 27.1 | 2,477 | 28.4 | 0.085 |
| Others                     | 2,035 | 70.0 | 1,035 | 73.6 | 879 | 71.0 | 899 | 71.7 | 1,356 | 72.9 | 6,235 | 71.6 | |

*P value of < 0.001
this study (8712) with higher rate among males than females (57.2% vs. 42.8%). The predominance of leukemia cases were in the age group (0–4 years), followed by the age group (5–9 years). In general, leukemia is considered one of the most kinds of cancer impacted on children, and statistical studies reported that the incidence of leukemia cases of children has higher rates over the globe. However, the occurrence of leukemia in the Saudi population was low when compared to developed countries such as United Kingdom, United States, Australia, Canada and Germany. [2] In the United Kingdom for example, Leukemia accounts of 34% of all malignancies in children aged under 15 years. A recent study from Piedmont reported that leukemia was the first cancer among children and adolescents in the years from 1967 to 2011, with a peak age was at 1–4 years (75.9%), similar to our findings [13]. Other study from Yemen (Aden Cancer Registry) stated that leukemia was of higher rate among boys and girls < 15 years old (34.2 and 38.3%, respectively), as well as more in men (10.5%) compared to women (7.6%) [14].

Worldwide, cancer incidence in children varies from 10 to 18 per 100,000 children under 15 years of age [15]. The cancer incidence in KSA increased throughout the years like other developing countries that could be due to the improvement of health care facilities, diagnostic procedures, and easy referral system for further diagnosis and treatment to well recognizable tertiary hospitals.

### Table 8

| Variables | Morphology | Children | Adults | Elderly | P value |
|-----------|------------|----------|--------|---------|---------|
|           | No.        | %        | No.    | %        | No.    | %        | P value |
| Precursor B-cell lymphoblastic leukemia | 1,215 | 36.6 | 388 | 10.2 | 27 | 1.7 | 0.001 |
| Precursor cell lymphoblastic leukemia, NOS | 1,043 | 31.4 | 404 | 10.6 | 58 | 3.6 | |
| Precursor T-cell lymphoblastic leukemia | 177 | 5.3 | 144 | 3.8 | 2 | 0.1 | |
| Acute myeloid leukemia, NOS | 250 | 7.5 | 554 | 14.6 | 236 | 14.8 | |
| Acute leukemia, NOS | 68 | 2.0 | 78 | 2.1 | 52 | 3.3 | |
| Acute monocytic leukemia | 55 | 1.7 | 126 | 3.3 | 53 | 3.3 | |
| Leukemia, NOS | 34 | 1.0 | 84 | 2.2 | 100 | 6.3 | |
| Acute myelomonocytic leukemia | 37 | 1.1 | 127 | 3.3 | 35 | 2.2 | |
| Acute myeloid leukemia with maturation | 45 | 1.4 | 91 | 2.4 | 30 | 1.9 | |
| Acute myeloid leukemia without maturation | 18 | 0.5 | 60 | 1.6 | 25 | 1.6 | |
| Acute promyelocytic leukemia, t(15;17)(q22;q11–12) | 61 | 1.8 | 220 | 5.8 | 34 | 2.1 | |
| B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma | 2 | 0.1 | 229 | 6.0 | 519 | 32.5 | |
| Chronic myelogenous leukemia, BCR/ABL positive | 4 | 0.1 | 86 | 2.3 | 17 | 1.1 | |
| Chronic myeloid leukemia, NOS | 59 | 1.8 | 875 | 23.0 | 197 | 12.4 | |
| All others | 250 | 7.5 | 333 | 8.8 | 210 | 13.2 | |
Other factor for the notified increase of cancer cases in Saudi population was the remarkable improvement in wealth, rapid transitional socioeconomic changes and lifestyle modifications, and thus increase in life expectancy at birth, contribute to the increase of cancer incidence in the country [6, 16]. Development of National Cancer Registry and improvement of registration practices with certified tumour registrars could be considered as additional factors lead to increase in the reporting of more cancer cases during the last years in the country. During the study period, the number of the population in Saudi Arabia have growing by 50% of the population in 1999 compared to the year 2013. This could also explain the increasing trend of leukemia incidence in the country [17].

The current study showed a variation in the distribution of the leukemic cases among Saudi population over the different regions of Saudi Arabian Kingdom. For example, the most reported cases were from the Central region of Saudi Arabia (33.6%), while the lowest rate was reported from Madinah region (14.3%). This could be explained as the fact that the Central region has several mega medical centers such as King Abdulaziz Medical City, King Faisal Specialist Hospital and Research Center, and King Fahd Medical City, all are considered as big referral hospitals that allowing the refer of cases from other regions to the central one. In addition, Riyadh as a capital of the Kingdom, accounte over 7 million people which is around 22% of the population of the whole country [8].

The present study showed that a patterned increase in the overall incidence of leukemia cases during the period (1999–2013) with higher incidence in males compared to females. Similar findings were reported by Jung et al., where the incidence of leukemia in South Korea raised from 4.7/100,000 in the year 1999 to 5/100,000 population in the year 2009 [18]. According to age groups, our findings showed less likely trend among adults those from 15 years through 60 years old in both genders. The current study is consistent with previous studies, which showed that elderly people over 60 year old has high risk...
for leukemic progression that could be due to immune system dysfunction or idiopathic causes. For example, in 2013, the incidence of leukemia cases in elderly patients (60–99 year old) was 12.0 (male) and 8.0 (female) per 100,000 person (Fig. 4) compared with adult patients (>14–59 year old) was 3.0 (male) and 1.8 (female) per 100,000 person (Fig. 3). The trend of leukemia cases over the study period have increased from 5.2% in 1999 to 7.9% in 2013, with no significant differences between males and females. Although, the relation of leukemia and cause is of great important in the public health field, this issue is not yet studied extensively in the country. The Kingdom of Saudi Arabia has went through a massive economic evolution after its entry in the petroleum industry, moreover, as a developing country, leukemia incidence has increased over decade due to several factors, such as: population growth, ageing, western life adoption, role of environmental factors, genetic risk factors and mony others. Both pre-natal and post-natal exposure to ionizing radiation (particularly X rays) can cause leukemia in children [19]. Pre-natal exposure to X rays has been greatly reduced with the adoption of ultrasound for screening in pregnant women. Several studies link pesticide exposure by both parents and children to leukemia. The pattern of disease suggests that some damage to chromosomes may occur before the child is born [20]. Children born to parents employed in certain occupations that have chemical exposures are more likely to have leukemia [21]. Chemicals, specifically including benzene, have been shown to cause leukemia in adults.

Among Saudi regions, the two most common leukemia subtypes were Precursor B-cell lymphoblastic leukemia followed by Precursor cell lymphoblastic leukemia, NOS. Moreover, the top three most common leukemia subtypes in both genders were: Precursor B-cell lymphoblastic leukemia, followed by Precursor cell lymphoblastic leukemia, NOS and Chronic myeloid leukemia, NOS. This trend in the subtypes of leukemia could also be found in different countries in the Gulf region like United Arab Emirates, Kuwait and Oman [6].

Limitations: Hence secondary data were used in this study, limitations are present due to the used method in data analysis. Moreover, the collection of data was not for the purpose of investigating the burden of leukemia in the Kingdom of Saudi Arabia. There were some inaccurate information in the data from SCR such as mistakes in age, nationality, and topography. For example, SCR report that the majority of leukemia cases were metastized where the leukemia is diseases of blood and no metastasis should be reported. In addition, The SCR did not register the demographic information of the patient such as marital status and occupation which could be risk factors for specific cancer.

Conclusion
Over the 15 years period, the trend of leukemia showed the likelihood of increase in rate particularly in males with highest incidence reported from the central region of Saudi Arabia which needs more investigation if cases were really from this region or focused around the capital Riyadh. According to the type of leukemia among the Saudi population, resources for diagnosis and treatment should be planned with more orientation toward the accurate diagnosis. As the “not specific diagnosis” is common among the reported data, more training and facilities should be provided to the health care facilities to bring a good early diagnosis and accordingly appropriate therapy with possible better standard of cure. Findings from the analyzed data based on cancer registries all over the country, still showed significant limitation in reporting standardized data on leukemia from the health care settings. To correct this part and bringing clean and clear data, training is very important to prepare certified tumor registrar over the country regions.
Abbreviations
ALL: Acute Lymphoblastic Leukemia; AML: Acute Myeloid Leukemia; CLL: Chronic Lymphocytic Leukemia; CML: Chronic Myeloid Leukemia; ICD-O: International Classification of Diseases for Oncology; KAIMRC: King Abdullah International Medical Research Centre; KSAU-HS: King Saud Bin Abdulaziz University for Health Sciences; MENA: Middle-East and Northern Africa; MOH: Ministry of Health; SCR: Saudi Cancer Registry

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Authors’ contributions
AB developed the idea and the project, analyzed the data, and drafted the manuscript; edited. NA, has contributed in analysis and writing the manuscript; AB, has contributed in analysis of the data and writing; MA, NA, and AS were contributed in writing and editing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
No need for informed consent because the used data was aggregation of secondary data. However, all the data received from the SCR were anonymous just with coded number and without any link to patient’s identity. The proposal of this study was approved by the research committee in the King Saud Bin Abdulaziz University for Health Sciences (KSAU-HS) and thereafter reviewed and approval by the research committee in the King Abdullah International Medical Research Centre (KAIMRC) in the ministry of National Guard Health Affairs, Riyadh, Kingdom of Saudi Arabia under the reference (SP 17/030/IR).

Consent for publication
Not applicable.

Competing interests
The author declares they have no competing interests.

Author details
1College of Public Health and Health Informatics, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. 2King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia. 3College of Dentistry, Aden University, Aden, Yemen. 4Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. 5King Abdullah International Medical Research Center (KAIMRC), Riyadh, Saudi Arabia.

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