SUNTEXT REVIEWS

SunText Review of Biotechnology
ISSN: 2766-5097

Open Access
Research Article
Volume 2:2

The Hematological Malignancies Incidence in Gaza Strip, Palestine

Khaled Abu Ali*, Japer MO, Al-Bayyouk NA, Shaqra MA, Shab RS and Al-Masri DH

Doctor of Public Health, Medical Laboratory Sciences, University College of Science and Technology, Palestine

***Corresponding author:** Khaled Abu Ali, Doctor of Public Health, Medical Laboratory Sciences, University College of Science and Technology, Palestine; E-mail: khaled_abuali@yahoo.com

Received date: 11 July 2021; **Accepted date:** 18 July 2021; **Published date:** 22 July 2021

Citation: Khaled Abu Ali, Japer MO, Al-Bayyouk NA, Shaqra MA, Shab RS, Al-Masri DH (2021). The Hematological Malignancies Incidence in Gaza Strip, Palestine. SunText Rev Biotechnol 2(2): 127.

DOI: https://doi.org/10.51737/2766-5097.2021.027

Abstract

Cancer is a major life-threatening disease worldwide. Approximately 9.6 million people died from cancer in 2018 worldwide. The lack of any nationwide leukemia screening program and raising awareness of the Palestinian population also plays a role in underlying late presentation and noncompliance with screening guidelines. Hence it is important for physicians and pathologists to determine the current burden of leukemia in Palestine. This study was a retrospective cross-sectional design started in Jul 2019 and finished in Aug. 2019. The study population was compromised of all participants in Jan 2017 - Jul 2019. Data gathered from governmental specialized hospitals in cancer (Al-Rantisi Hospital for Cancer, Al Europe Hospital) from patients' medical records. The total number of cases was 285. The incidence rate was 15 cases per 100,000 and the annual incidence was 107 case. 28% of the cases with the most cases of Hematological Malignancies were acute lymphocytic leukemia and most of them affect the age groups are children aged 1-18 years. This is followed by Hodgkin disease, which affects males more than females and affects adult and old age groups. The third is multiple myeloma, which is the most common condition that affects old age. Then the non-Hodgkin disease and affects females more than males. The incidence of lymphoid lineage was 85% and myeloid lineage was 12%. There was a considerable difference in the incidence of Hematological malignancies, by age groups.

Keywords: Blood cancer; Cancer; Leukemia; Malignancy

Introduction

Cancer is a generic term for a large group of diseases characterized by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to other organs. Other common terms used are malignant tumors and neoplasms [1,2]. Cancer can affect almost any part of the body and has many anatomic and molecular subtypes that each require specific management strategies [3]. Cancer is a major life-threatening disease worldwide. Approximately 18.1 million patients were newly diagnosed with cancer and 9.6 million people died from cancer in 2018 worldwide [4]. According to Globocan 2018 statistics computed using sex-; site- and age-specific incidence to 1-; 3- and 5-year prevalence ratios from Nordic countries for the period (2000-2009), and scaled using Human Development Index (HDI) ratios. Reported cases of cancer in Palestine was 4,499 new cases, official statistics of World Health Organization (WHO) revealed that the rate of cancer in Gaza Strip and West Bank reached 89 new cases per 100,000 population. The Globocan 2018 added that 53.2% of new cancer cases registered among Palestinians are females, and 46.8% are males, and the rat of death by cancer was reported 52 death per 100,000 Population [3]. Furthermore, the Ministry of Health of Palestine (MOHP) in 2015, the total number of reported cases of cancer in Palestine was 3,927 new cases. Moreover, Hematological Malignancy (H. M.) was the most common type of cancer in children in Palestine and 30.2% of the total cancer recorded in children. In the past three years, cancer in Palestine has been the second largest cause of death among Palestinians after cardiovascular disease, after being the third most important cause of death in Palestine for many years. According to the Ministry of Health, Palestinian deaths from cancer accounted for

13.8% of all deaths. In the Gaza strip, the cancer mortality rate was 13.2% of all deaths, and in the West Bank 14.1% of all deaths [5]. Leukemia is a generic term for malignant diseases characterized by an uncontrolled proliferation of immature blood cells. These cells originate from a hematopoietic stem cell mutation and can lead to bone marrow failure and end up in death [6]. Leukemia is the general term for some different types of blood cancer. There are four main types of leukemia called: 1. acute lymphoblastic (lymphocytic) leukemia (ALL), 2. Acute myeloid (myelogenous) leukemia (AML), 3. Chronic lymphocytic leukemia (CLL), 4. Chronic myeloid (myelogenous) leukemia (CML) [7]. However, The Global Cancer Observatory from WHO report H.M. was 15.0% of total malignant neoplasm, the 5.6% of the cancer was Leukemia, but without any categorization in the report or in the Ministry of health annual report of Palestine, also Non-Hodgkin lymphoma 5.2%, Hodgkin lymphoma 2.2%, Multiple myeloma 2.0% [3-5]. According to illustrate the Incidence and mortality rate are almost equal (7.7 to 6.7) per 100, 000, the mortality rate of Non-Hodgkin lymphoma is 4.5 less than the incidence rate of 8.2. In addition, the highest critical mortality was in Breast cancer, and the lowest was Thyroid cancer. Due to the lack of any nationwide H.M. screening program, the majority of the population of Palestine is still unaware of this blood disorder. Hence, it is important for the physicians and pathologists to determine how the occurrence and outcome of the disease differ across the whole Gaza strip (Figure 1).

Objectives

General objective

In this context, the aim was to Measure Morbidity and Mortality Frequency of Hematological Malignancies and the percentage of their applied Laboratory tests in Gaza strip, Palestine.

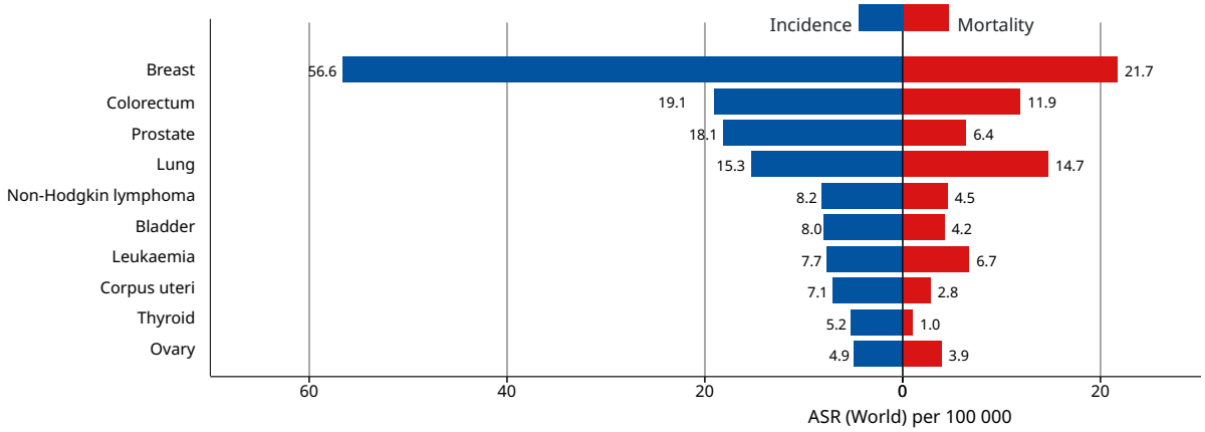

Figure 1: *Age Standerdized(World) incidence and mortality rates, top 10 cancers in Gaza strip and Westbank. "The Global Cancer Observatory - All Rights Reserved - May, 2019." [3] [3] [3].*

Specific objectives

To determine the incidence and the prevalence of Hematological Malignancies categories.

- To verify types of specified applied tests for Hematological Malignancies patients.
- To determine the shortage in required laboratory tests for Hematological Malignancies.
- To calculate the mortality rate for each disease.
- To calculate of survival rate in each disease.

Significance

According to incidence of cancer in Gaza Strip and West Bank reached 89 new cases per 100,000 population in Addition to Hematological Malignancy is the most common type of cancer in children in Palestine and 30.2% of total cancer recorded in children, high percentage of deaths among Hematological Malignancy which is 15.9% of the total number of deaths by cancer. Due to the lack of any nationwide Hematological Malignancy screening program especially Leukemia, the majority of the population of Palestine is still unaware of this blood disorder. Lack of awareness also plays a role in underlying late presentation and noncompliance with screening guidelines. Hence, it is important for the physicians and pathologists to determine the current burden of leukemia's in Gaza strip [8].

Literature Review

Normal hematopoiesis

Blood cells develop through a process called haematopoiesis. This involves bone marrow and part of the lymphatic system. Bone marrow contains unspecialized cells known as haematopoietic stem cells. As they divide and mature, they become more specialized and develop into one of the three types

of blood cell, each with a specific function. Blood cells only last for a limited period of time, and so they constantly need to be replaced in the correct numbers to meet the body's needs. One of the key functions of the spleen is to remove worn out blood cells from circulation. An additional component of blood is plasma (Figures 2 and 3).

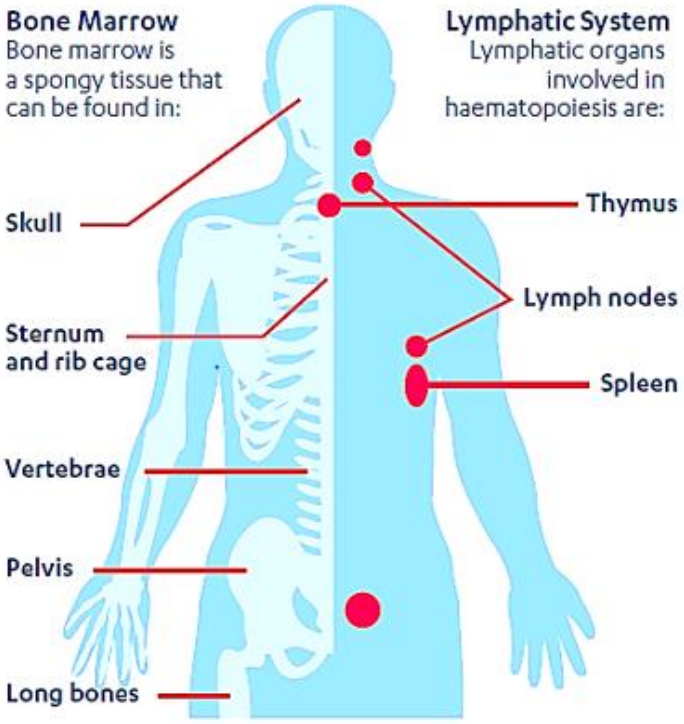

Figure 2: *Bone Marrow and Lymphatic System locations in human body.*

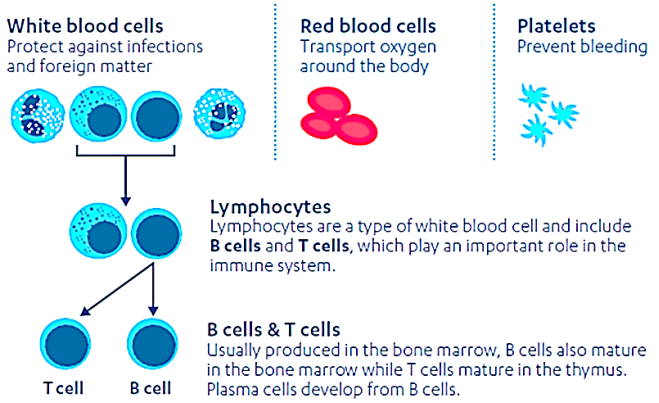

Figure 3: *Illustrate Different Blood components with their function.*

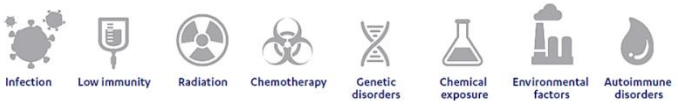

Figure 4: *Etiology of Cancer.*

What causes blood cancer

To function properly, the body needs to produce exactly the right amount of each type of blood cell. Blood cancers develop when damage occurs to vital genes, disrupting the normal lifecycle of blood cells, and upsetting this balance. Risk factors include as (Figure 4) shown:

What are the symptoms of blood cancer

Many symptoms of blood cancer are a result of fewer healthy, functioning blood cells, or overproduction of abnormal cells, causing a lack of space where blood cells are produced, i.e. bone marrow and the lymphatic system as presented in (Figure 5).

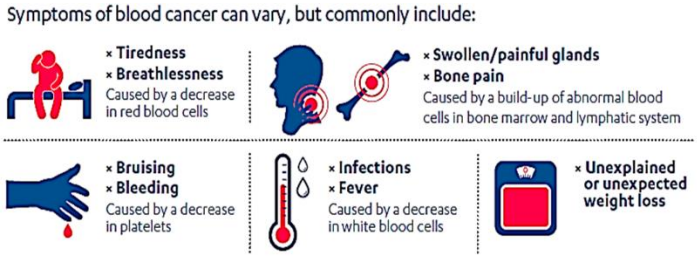

Figure 5: *Most Common Blood Cancer Symptoms*

How are blood cancers classified

There are different types of blood cancer, which can be classified in three main groups as illustrated in (Figure 6):
Other blood disorders closely related to blood cancers and that may develop into leukemia, include:

- Myelodysplastic syndrome: Some blood cells made in the bone marrow are damaged resulting in a lack of healthy blood cells being released into the bloodstream.
- Myeloproliferative neoplasm: Too many of one or more types of blood cell are made in the bone marrow.

WHO 2008 classification

WHO classification of myeloid neoplasms:

- The myeloproliferative neoplasm (MPNs), including the myeloid and lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB, and FGFRA
- The acute myelogenous leukemia (AML)
- The myelodysplastic syndromes (MDS)
- The MDS/ MPN syndromes [1,2]

Classification of lymphoid neoplasms:

WHO classification of precursor lymphoid neoplasms [2]

- B lymphoblastic leukemia/lymphoma
- B lymphoblastic leukaemia/lymphoma, NOS
- B lymphoblastic leukaemia/lymphoma with recurrent genetic abnormalities
- B lymphoblastic leukaemia/lymphoma with (9;22)(q34;q11.2);BCR-ABL1

- B lymphoblastic leukaemia/lymphoma with t(v11q23);MLL rearranged
- B lymphoblastic leukaemia/lymphoma with t(12;21)(p13;q22) TEL-AML1 (ETV6-RUNX1)
- B lymphoblastic leukaemia/lymphoma with hyperdiploidy
- B lymphoblastic leukaemia/lymphoma with hypodiploidy
- B lymphoblastic leukaemia/lymphoma with t(5;14)(q31;q32) IL3-IGH
- B lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13.3);TCF3-PBX1
    - T lymphoblastic leukaemia/lymphoma

➢ **WHO (2008) Classification Schemes for the Acute Myelogenous Leukemias [1,2]**
With recurrent genetic abnormalities With t(8;21)(q22;q22) With inv(16)/t(16;16)(p13.1;q22) With t(15;17)(q22;q12) With t(9;11)(p22;q23) With t(6;9)(p23;q34) With inv(3)/t(3;3)(q21;q26.2) With t(1;22)(p13;q13) With mutated NPM1 (provisional) With mutated CEBPA (provisional)
With myelodysplasia related changes Previous history of MDS Multilineage dysplasia MDS-related cytogenetic abnormalities
Therapy-related myeloid neoplasms t-AML/t-MDS (t-MN)
Not otherwise specified With minimal differentiation Without maturation With maturation Myelomonocytic leukemia Monoblastic leukemia Monocytic leukemia Erythroleukemia Erythroid myeloid type Pure erythroid Acute megakaryoblastic leukemia Acute basophilic leukemia Acute panmyelosis with myelofibrosis
Myeloid sarcoma
Myeloid leukemia associated with Down syndrome
Blastic plasmacytoid dendritic cell tumor

French–American–British (FAB, 1985)	Cytogenetic	WHO (2001)	WHO (2008)	WHO (2016)
M0: AML with minimal differentiation	**Favorable**	**Genetic**	**With recurrent genetic abnormalities**	**With recurrent genetic abnormalities**
	t(8;21)	t(8;21)	With t(8;21)(q22;q22)	AML with t (8;21)(q22;q22.1);RUNX1-RUNX1T1
M1: AML without maturation	inv(16)/t(16;16)	t(inv(16)/t(16;16)	With inv(16)/t(16;16)(p13.1;q22)	AML with inv(16)(p13.1q22) or t(16;16) (p13.1;q22);CBFB-MYH11
M2: AML with maturation	t(15;17)	t(15;17)	With t(15;17)(q22;q12)	
M3: APL	**Intermediate**	t(v;11q23)	With t(9;11)(p22;q23)	APL with PML-RARA
M3v: microgranular variant	Normal	**AML with dysplasia therapy related AML**	With t(6;9)(p23;q34)	AML with t(9;11)(p21.3;q23.3);MLLT3-KMT2A
M4: AMML	+8		With inv(3)/t(3;3)(q21;q26.2)	AML with t(6;9)(p23;q34.1);DEK-NUP214
M4eo: AMML with abnormal eosinophils	t(v;11q23)	Etoposide	With t(1;22)(p13;q13)	AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2, MECOM
	del(7q)	Cytotoxic or radiation	With mutated NPM1 (provisional)	
M5a: acute monoblastic leukemia	+21	**Not otherwise specified**	With mutated CEBPA (provisional)	AML (megakaryoblastic) with t(1;22) (p13.3;q13.3);RBM15-MKL1
	+22	With minimal differentiation	**With myelodysplasia related changes**	
M5b: acute monocytic Leukemia	Other	Without maturation	Previous history of MDS	Provisional entity: AML with BCR-ABL1
	Adverse	With maturation	Multilineage dysplasia	AML with mutated NPM1
M6: erythroleukemia	del(5q)	Myelomonocytic leukemia	MDS-related cytogenetic abnormalities	AML with biallelic mutations of CEBPA
M7: acute megakaryoblastic leukemia	-5	Monoblastic leukemia	**Therapy-related myeloid neoplasms**	Provisional entity: AML with mutated RUNX1
	-7	Monocytic leukemia	t-AML/t-MDS (t-MN)	**AML with myelodysplasia-related changes**
	Complex	Erythroleukemia	**Not otherwise specified**	**Therapy-related myeloid neoplasms**
	abn (3q)	Erythroid myeloid type	With minimal differentiation	**AML, NOS**
		Pure erythroid	Without maturation	AML with minimal differentiation
		Megakaryoblastic	With maturation	AML without maturation
			Myelomonocytic leukemia	AML with maturation
			Monoblastic leukemia	Acute myelomonocytic leukemia
			Monocytic leukemia	Acute monoblastic/monocytic leukemia
			Erythroleukemia	Pure erythroid leukemia
			Erythroid myeloid type	Acute megakaryoblastic leukemia
			Pure erythroid	Acute basophilic leukemia
			Acute megakaryoblastic leukemia	Acute panmyelosis with myelofibrosis
			Acute basophilic leukemia	**Myeloid sarcoma**
			Acute panmyelosis with myelofibrosis	**Myeloid proliferations related to Down syndrome**
			Myeloid sarcoma	Transient abnormal myelopoiesis (TAM)
			Myeloid leukemia associated with Down syndrome	Myeloid leukemia associated with Down syndrome
			Blastic plasmacytoid dendritic cell tumor	

AML, Acute myeloid leukemia; *AMML*, acute myelomonocytic leukemia; *APL*, acute promyelocytic leukemia; *WHO*, World Health Organization.

Classical hodgkin lymphoma

Nodular sclerosis classical Hodgkin lymphoma.
Classical Hodgkin lymphoma
Lymphoticyte rich classical Hodgkin lymphoma.
Mixed cellularity classical Hodgkin lymphoma.
Lymphocyte – depleted classical Hodgkin lymphoma [1,2].

WHO classification of Mature B-Cell Neoplasms

- Chronic lymphotic leukemia / small lymphocytic lymphoma
- B-cell prolymphocytic leukemia
- Splenic marginal zone lymphoma
- hairy cell leukemia
- Splenic lymphoma
- Splenic diffuse red pulp small B-cell lymphoma
- Hairy cell leukemia variant
- lymphoplasmacytic lymphoma
- weldenstrom macroglobulinemia
  - αHeavy chain disease
- plasma cell myloma

- solitary plasmacytoma of bone
- Extraosseous plasmacytoma
- Extranodal marginal zone lymphoma of MALT lymphoma
- Nodal marginal zone lymphoma
- pediatric nodal marginal zone lymphoma
- Follicular lymphoma
- pediatric folicular lymphoma
- Primary cutaneous follicle center lymphoma
- Mantle cell lymphoma
- DLBCL, NOS
- Tcell/histiocyte- rich large B-cell lymphoma
- primary DLBCL of the CNS
- Primary cutaneous DLBCL , leg type
- EBV-positive DLBCL of the elderly
- DLBCL associated with chronic inflammation
- lymphomatoid granulomatosis
- primary mediastinal (thymic) large B-cell lymphoma
- intravascular large B-cell lymphoma
- ALK – Positive large B-cell lymphoma
- plasmablastic lymphoma
- Large B-cell lymphoma arising in HHV8-associated multicentric castleman disease
- Primary effusion lymphoma
- B-cell lymphoma unclassifiable with feature intermediate between diffuse large B-cell lymphoma and classical Hodgkin lymphoma
- Burkitt lymphoma
- B-cell lymphoma , unclassifiable , with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma

WHO Classification of Mature T-Cell and NK-Cell Neoplasms

- T-cell prolymphocytic leukemia
- T- cell large granular lymphocytic leukemia
- chronic lymphoproliferative disorder of NK cells
- aggressive NK cell leukemia
- systemic EBV-positive T-cell lymphoproliferative disease of childhood
- hydroa vacciniforme – like lymphoma
- adult T-cell leukemia
- Extranodal NK/Tcell lymphoma , nasal type
- Enteropathy associated T-cell lymphoma
- Subcutaneous panniculitis – like T-cell lymphoma
- Mycosis fungoides
- Sezary syndrome
- Primary cataneous CD 30 T-cell lymphoproliferative disorders
- lymphomatoid papulosis
- primary cutaneous anaplastic large- cell lymphoma
- primary cutaneous T-cell lymphoma
- primary cutaneous aggressive epidermotropic CD8 cytotoxic T-cell lymphoma
- primary cutaneous small/ medium CD4 T-cell lymphoma
- peripheral T-cell lymphoma NOS
- Angioimmunoblastic T-cell lymphoma
- Anaplastic large –cell lymphoma ALK +ve
- Anaplastic large-cell lymphoma ALK –ve

WHO Classification of Histiocytic and Dendritic Cell Neoplasms

- Histiocytic sarcoma
- Langerhans cell histiocytosis
- Langerhans cell sarcoma
- Interdigitating dendritic cell sarcoma
- Follicular dendritic cell sarcoma
- Fibroblastic reticular cell tumor
- Intermediate dendritic cell tumour
- Disseminated juvenile xanthogranuloma
- Dendritic and histiocytic neoplasms are hematologic malignancies that have distinct yet variable clinical presentation, and together they make up less than 1% of the neoplastic process of the lymph node or soft tissue [9]. However, the true prevalence of these disorders remains uncertain because many have been recognized only recently. Several entities are recognized in the 2008 WHO classification of histiocytic and dendritic cell neoplasms.

Leukemia

Leukemia is a type of cancer arising from any group of blood cancers that usually begin in the bone marrow and result in high numbers of abnormal blood cells. Maybe white blood cells (WBCs) leukemia resulting from malignant transformation of different types of white blood cell precursors: lymphocytic leukemia is an overproduction of lymphocytes, and myeloid leukemia is an overproduction of myelocytes [10-12]. Leukemic cells grow and divide uncontrollably, displacing healthy blood cells. This can lead to serious problems such as anemia, bleeding, and infection [10-14]. Leukemia is the fifth leading cause of cancer death in the United States, and the majority of cases occur in older adults. Leukemia is more common in men than women and in 2019, it is estimated that there will be 61,780 new cases of leukemia and an estimated 22,840 people will die of this disease

[15]. Leukemias are also classified as either acute or chronic, depending on how quickly they progress [7,10-12]. Acute Leukemias, if left untreated, progress very rapidly, and without proper care the mortality rate is extremely high within several months of diagnosis. However, appropriate treatment can considerably improve prognosis and survival times for acute leukemia patients, and many can be cured [10]. Chronic Leukemias, on the other hand, may not cause any significant problems before diagnosis, though sometimes they cause nonspecific symptoms such as weight loss, fatigue, or abdominal pain. In many cases, abnormal blood cell counts found during routine blood work in people without symptoms may prompt a physician to suspect leukemia, which can be confirmed with further testing [10]. Researchers are making great headway in the battle against leukemia. Innovative strategies including antibody-based therapies, interventions directed at leukemia stem cells, and novel targeted agents have shown promise in preliminary research and early clinical trials [16-20]. Moreover, evidence suggests that some integrative interventions may complement conventional leukemia therapies. Several medicinal plants are excellent sources of chemo preventive phytochemicals that have been shown to be active against various leukemia cell lines, and some may modulate molecular targets known to be involved in leukemia development and progression [21,22].

Types of leukemia

Leukemia is categorized on the basis of how long the disease takes to progress and the kinds of blood cells affected. Acute leukemia usually presents suddenly, and patients often develop symptoms right away. Chronic leukemia progresses slowly and may not cause symptoms for years [14,23]. Lymphocytic leukemia affects "T" and "B" white blood cells known as lymphocytes. Myeloid leukemia affects myeloid cells, which go on to form white blood cells other than lymphocytes (granulocytes and monocytes), red blood cells, and platelets. Leukemia is classified into four main types: acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML) [14,23]. There are several other types of leukemia as well, such as hairy cell leukemia, chronic neutrophilic leukemia, and acute megakaryocytic leukemia, but these are relatively rare [24]. Rounded to the nearest 10; the numbers depict estimated new cases of leukemia in the United States in 2014. Leukemias are further classified into subtypes depending on the molecular and genetic characteristics of leukemia cells. Correctly identifying the properties of each patient's cancer is critical for prognosis and treatment [14,17,24,28].

Laboratory Tests of Hematological Malignancies

Components in the routine clinical evaluation of myeloid diseases current

- Accurate clinical history, including family history and physical examination findings
- General laboratory findings, including CBC, and other specific tests (e.g., EPO) when appropriate
- Evaluation of well-prepared and stained peripheral blood smear with 200 cell differential count
- Review of BM aspirate, including iron stain, and 500 cell differential count
- Evaluation of H&E sections of BM biopsy of sufficient length and reticulin stain
- Phenotyping studies, including cytochemical reactions (nonspecific and specific esterase reactions and myeloperoxidase) and flow cytometric analysis of peripheral blood or BM for phenotype of blasts or other cells when appropriate
- Cytogenetic analysis, including karyotype, and FISH for specific abnormalities when appropriate
- Single-nucleotide polymorphism array karyotyping
- Genetic analysis for particular genetic rearrangements or mutations, including gene sequencing when appropriate
- Next-generation sequencing
- Potential Future Clinical Studies
- Gene expression arrays
- Genome-wide epigenetic studies
- BM, Bone marrow; CBC, complete blood count; EPO, erythropoietin; FISH, fluorescence in situ hybridization; H&E, hematoxylin and eosin [1].

Related Studied

MOHP demonstrates in the 2018 report on 2011-2016 period there were 8515 cases of malignant neoplasm; the third-highest percent was Leukemia were 9.1% about 775 cases, Lymphoma 6.2% about 528 cases, and it was the fourth-highest in female malignancies with 5.3% of 4705 female cases [29].

In addition to the incidence of Malignancy in children's ages, 18 years (yrs) and less were 608 approximately 7.1% from the total malignant neoplasm; the percentage of leukemia was 23.8%, and the highest percentage was Lymphoma 17.1% in children [29]. On the other hand, the second leading cause of death according to the report of MOHP for deaths was malignancy neoplasm; counted 805 death about 10.6% of total causes. Furthermore the Mortality rate 36.8/100000 of the population of in the end 2018; the percentage of deaths according age groups 1-less than 5yrs 5.3%, from 5- less than 20yrs 5.8%, from 20- less than 60yrs 16.7% and the second-highest percent of total deaths in the age group more than 60yrs 10.2% from the total 2956 deaths [30]. Finally, according to MOHP report the shortage in the annual financial needs for laboratory expenses were 26.9% of the essential requirements [29]. In India, a study by Sharique et al.,2016 evaluated the frequencies of ALL, AML, CLL and CML,

diagnosed in our hospital. Study also aimed at calculating frequencies as per World Health Organization (WHO) classified leukemia on the bone marrow studies and found that An upward trend in incidence of leukemia with age was seen, although the acute leukemia's were more common in patients below 20 years of age. The total number of males who participated in this study were 116[40.6%] while females were 170[59.4%]. Maximum patients were in the age group 21-30 years. The prevalence percentage of leukemia seen in our study was more in the age group of 51-60 and 71-80 years. Males were seen to be afflicted more than females in all age groups. No correlation between the gender of the patients and type of leukemia was seen on applying Fischer Exact test. Acute leukemia show a greater prevalence in second decade [8]. In Germany, across-sectional study was conducted to evaluate the oral health of adult patients with newly diagnosed acute leukemia, the study showed that Thirty-nine patients with leukemia (AML 26, ALL 13) and 38 HCs were included. Oral mucosal findings were present in 62% of L compared to 0% of HC patients, whereby gingival hyperplasia was the most detected finding. Furthermore, a higher caries prevalence in leukemia patients was shown (D value 3.64 ± 3.98 vs. 0.72 ± 1.72, $p < 0.01$). The periodontal parameters were poorer in leukemia patients. No substantial differences in microbiological findings of selected bacteria were detected within L group and between Leukemia and Healthy Control patients [6]. In America, a study by Jorge et al .,2012 estimate the increasing prevalence and plateau prevalence of CML in future years and found that On the basis of these calculations, the mortality ratio of patients with CML compared with an age-matched normal population was approximately 1.53. The estimated prevalence of CML is approximately 70,000 in 2010, 112,000 in 2020, 144,000 in 2030, 167,000 in 2040, and 181,000 in 2050, when it will reach a near plateau prevalence [31]. In India, Radha et al. 2014 conducted their study to find out geographic pattern of leukemia and its distribution throughout the Haryana and he observed that 51% patients were suffering from acute forms of leukemia while 49% suffered from chronic type. Leukemia was more frequently observed in adults. Male to female ratio was 2:1 and majority of the patients (88.92%) belonged to six districts (i.e. Rohtak, Jind, Bhiwani, Sonipat, Jhajjar, Hissar) [32]. Kyu-Won et al. study presents the 2014 nationwide cancer statistics in Korea, including cancer incidence, survival, prevalence, and mortality and he observed that in 2014, 217,057 and 76,611 Koreans were newly diagnosed and died from cancer respectively. The ASRs for cancer incidence and mortality in 2014 were 270.7 and 85.1 per 100,000, respectively. The all-cancer incidence rate has increased significantly by 3.4% annually from 1999 to 2012, and started to decrease after 2012 (2012-2014; annual percent change, –6.6%). However, overall cancer mortality has decreased 2.7% annually since 2002. The 5-year relative survival rate for patients diagnosed with cancer between 2010 and 2014 was 70.3%, an improvement from the 41.2% for patients diagnosed between 1993 and [33] (Figures 7-14).

Materials and Methods

Study design

The study design was a retrospective cross-sectional study.

Study population

The study population was comprised of any participants Jan 2017- Aug 2019.

Study period

The study was started in Jul 2019 and finished in Aug. 2019.

Sampling

We was collected data from governmental specialized hospitals in cancer (Al-Rantisi Hospital for Cancer, Al Europe Hospital) from medical record.

Inclusion and Exclusion criteria

Inclusion criteria: any Cancer Patient with Hematological Malignancies, Myeloid or Lymphoid Lineage from Gaza strip included.

Exclusion criteria: other cancer patients, or non-malignant patients.

Ethical Consideration

An authorization to carry out the study will obtained from the local ethics committee using an agreement letter.

Tools of the Study

Data collection

Data gathered from Medical Record in Governmental Hospitals; Hematological Malignancies Type, all tests used in the diagnosis and in follow up.

Components in the routine clinical evaluation of myeloid and lymphoid malignances routine tests

- Primary
- BM, Bone marrow analysis; Evaluation cell differential count
- CBC, complete blood count; Evaluation cell differential count.
- Other specific tests; (EPO) erythropoietin test.

Phenotyping studies:

- Cytochemical reactions (nonspecific and specific esterase reactions and myeloperoxidase)
- Flow cytometry analysis
- Protein Electrophoresis
- Immunological Phenotyping

Cytogenetic analysis, including

- karyotype
- FISH for specific abnormalities when appropriate

Molecular Genetic analysis for

- Single-nucleotide polymorphism array karyotyping,
- particular genetic rearrangements or mutations,
- including gene sequencing when appropriate
- Next-generation sequencing

Potential Future Clinical Studies

- Gene expression arrays
- Genome-wide epigenetic studies

In addition to the date of diagnosis, age, where they are from and their gender.

Data Analysis

By using IBM SPSS, analysis software 20 to study the relationships by using Chi-square test and with Microsoft Excel 2016 determined the prevalence, incidence, and Mortality rate of each Malignancy, and the percentage of the most required tests applied for the patients.

Results

General incidence of hematological malignancies

The total Hematological Malignancies (H.M.) were 285 cases, nine of them were unclassified. However, the diagnosis of the rest, it did not subclassify some types that needed too, such as AML, ALL and Myeloproliferative Neoplasms. According to the study period, the population of Gaza strip in the middle of 2018 was 1932843 as mentioned by the Palestinian Central Bureau of Statistics (PCBS). The incidence rate of H.M. for 100000 People were about 15 cases, on the other hand, the annual incidence was 107 cases. The lowest age was 1 year however, the oldest age was 87 years, ALL was the highest annual incidence reach 28.8 % of the total H.M, followed by Hodgkin disease, Multiple Myeloma, and Non-Hodgkin disease with the respect percentage (18.9%, 13%, 9.8%). as mentioned in (Table 2), Also the lowest percent was for Hairy cell leukemia approximately 0%. These as illustrated in. We notes from this (Table 3) that children are the most affected age groups with ALL, especially the category 0-9 years 82 %, in contrast to its presence in adults (19-27, 28-36, 46-54) and less old age groups(55-63, 64-72). Hodgkin disease is most prevalent in adults aged 19-27, 37-45 years with 62.1%, 46.7% respectively. Burkitt's lymphoma appeared in children aged 18-10 with seven cases. It also appeared in adults aged 53-55 with one case. Follicular lymphoma appeared only in adult categories (37-45, 46-54, 55-63) with total percent of 1.4% of all H.M. Multiple myelomas the highest incidence in the older age group 82-90 years with 40% and 64-72 with 34.5%. Followed by the older adult group 46-54 with 30.6%. In addition, there was a highly statistically significant association between types of H.M. and the distribution according to the age groups as shown in table with P-value 0.000.Furthermore, the and 4.4 illustrate the disruptions of the H.M. between the classification of Age groups as Children (1-18) years, Adult (19-54) years and Old Age older than 55 years. There was a highly statistically significant association between types of H.M. and the distribution according to the age groups Classes with P-value 0.000. Firstly, in child group, the highest disease is ALL 68% of all H.M attacks children, followed by Hodgkin disease 12%, Burkitt's lymphoma 7% and AML 6%. Meanwhile, the highest percent 32% of the adult group was Hodgkin disease, followed Multiple myelomas 16%, Non-Hodgkin disease 15%. The lowest Percent goes for CLL, AML, Follicular lymphoma and Myeloproliferative Neoplasms. Lastly, among Old Age group, 16% was Multiple myelomas, it was the highest present, followed by Hodgkin disease, Non-Hodgkin disease, and CLL, the lowest incidence were Burkitt's lymphoma, Follicular lymphoma, and Hairy cell leukemia. Furthermore, 84.6 % of H.M. were myeloid lineage, otherwise 12.3% were lymphoid, and the unclassified was 3.2% as shown in table 4.3 and. There was no statistically significant association between H.M. and the Lineage distribution according to the age groups with P-value 0.269.The relationship between gender Male (M) and Female (F) with H.M. types was no statistically significant association, the P-value 0.086 as presented in table 4.4.The highest incident of H.M. in both genders was ALL, Hodgkin disease, multiple myeloma and Non-Hodgkin disease in descending order, however, the male higher than female as 45, 37 cases ALL respectively. In the same of ALL the Hodgkin disease and multiple myeloma but in Non-Hodgkin disease the female cases 18 higher than male 10 cases as illustrated in. In addition to CML, CLL and Burkitt's lymphoma was male higher than Female but lower incidence. Otherwise, the female was higher than in AML but with low incidence, in some H.M. like Hairy cell leukemia and Myelodysplastic/Myeloproliferative Neoplasms exclusively attacks female. Finally, there was not statistically significant relationship between the gender male and female with H.M. myeloid, lymphoid lineage, the P-value 0.821 as presented demonstrates the lymphoid lineage in female was higher than male but myeloid lineage approximately equal in both genders. After evaluation, medical record of Hematological Malignancy Patients for these components in the routine clinical evaluation of Myeloid and Lymphoid Malignancies applied for them in Gaza

strip hospitals or transferred to other hospitals outside Gaza strip. We found 28% of routine tests, in general, applied for the patients outside Gaza strip, but unfortunately, there had not done any test of Potential Future Clinical Studies in Gaza neither outside Gaza strip. In addition to the highest percent 50% of applied tests for Hodgkin Lymphoma, However the best percent for other listed diseases did not exceed 33%. Furthermore, most of the applied test of a routine test does not applied in Gaza strip Hospitals.

Discussion

Comparing the results with related studies

According to results demonstrated leukemia was 43.9% of hematological Malignancies in Gaza strip, which included ALL, AML, CLL, and CML, the highest percent of Leukemia in children less than 18yrs was for ALL and AML. in addition the lymphoma in children was 22% includes Hodgkin disease, Burkitt's lymphoma, Non-Hodgkin disease, and lymphoma, that correspond the towering percent of leukemia 23.8% and lymphoma 17.1% of malignancies neoplasm in children reported by MOHP, that had been published lastly in July 2019 for the study period 2011-2016 [29].

The demonstrated results were considerably greater than findings of WHO Globocan 2018 reported for Gaza strip and Westbank, where Leukemia 37.3% of hematological Malignancies, which was 15% of total malignancies neoplasm, however, they have coincided with leukemia was the highest incident in hematological Malignancies. In another hand, the incidence of Non-Hodgkin disease in Gaza strip was 9.8% distinguishable from WHO Globocan 2018 reported 34.7%, but Hodgkin disease 18.9% higher than 14.7% for Gaza strip and Westbank. Meanwhile, Multiple Myeloma has been compatible with the percentage of 13% [3,4]. Table 4.2 has identified the results and there was a highly statistically significant association between types of H.M. and the distribution according to the age groups that were consistent with the study of an estimation new cases of leukemia in the United States (US) in 2014. however, the highest ALL in children, it differs in the beak was 83% in the age group 1-9 yrs in contrast the US ages 3-7yrs [14, 17, 24, 32]. The US study was compatible with the increasing incidence of CLL in older adult and old age group, CML increased in Middle-aged adults, rarely children contrary to Gaza strip incidence of CML increased in old age group, older adults and rarely children [14, 17, 24, 32]. Lastly, AML in the US was mostly in adult and typically over age 40yrs contrary to Gaza strip study the highest percentage was in the children group [14, 17, 24, 32]. The study was compatible with the Indian Ahmed et.al study in 2016 the increase of acute leukemia in ages under 20yrs, and there was a statistically significant association between types of H.M and age groups. Although the Indian Rathee et.al study compatible with the finding in table 4.5 the highest incident of H.Ms were in Male, it was distinct in the difference between male and female [8, 32]. Interestingly the Germany study consistent with illustrated results in (Figure 8), where was ALL the highest among children [6]. Finally, according to results presented in (Figure 15) the percentage of applied routine tests for H.Ms was 28%, most of these test not included in list of tests available for the patients in Ministry of Health (MOH) at Gaza strip, particularly Flow cytometry analysis, Protein Electrophoresis, Immunological Phenotyping, Cytogenetic analysis, including and Molecular Genetic analysis based on MOHP 2018 report. That explained the increases of the mortality rate of leukemia in Gaza strip between different age groups the peak was in older ages over 60yrs as reported by MOH for deaths in Gaza strip 2018 [29].

Study limitations

The most important problem in demonstrates prevalence, mortality rate and survival rate for each Hematological Malignancy was the lack of cooperation of the information systems staff in the Ministry of Health (MOH) in Gaza to obtain the necessary data for the research. and Consequently to the rejection of the permeation request from the central public archive for dead patients in MOH, due to lack of an easy system to obtain the necessary data, which lead to substantial work pressure on, the employees, in addition to the research jest for Bachelor degree.

Conclusions and Recommendations

Conclusion

Based on the research data, the conclusion could be:

- There was considerably difference in the incidence of Hematological malignancies, by age groups and age Classes.
- There was no significant relationship between Hematological malignancies, gender and Hematological lineage myeloid or lymphoid of malignancy.
- The Gaza strip Hematological malignancies patients extremely lacks specialized routine medical laboratory tests generally, in particularly Phenotyping studies, Cytogenetic analysis, and Molecular Genetic analysis.

Recommendations

- New research questions emerge as a result of these findings. What are the causes of increasing types of Hematological malignancies with particular age groups? What are the

effects of immune disorders in (ALL) patients on increasing the chance of occurrence? Why are Hematologic malignancies in males more than females, is does genetically causes?

- We call on the Ministry of Health to improve medical laboratory services for patients in their diagnosis and follow-up which they are considered from routine tests:
- **Phenotyping studies**:
- Cytochemical reactions (nonspecific and specific esterase reactions and myeloperoxidase)
- Flow cytometry analysis
- Protein Electrophoresis
- Immunological Phenotyping
- **Cytogenetic analysis**, including
- karyotype,
- FISH for specific abnormalities when appropriate
- **Molecular Genetic analysis** for
- Single-nucleotide polymorphism array karyotyping,
- particular genetic rearrangements or mutations,
- including gene sequencing when appropriate
- Next-generation sequencing
- Improving the archiving system at MOH for clinical patients to be easier and more applicable for Doctors, MOH administration and researchers.
- Determining survival and mortality rate for each Hematological Malignancy.

Abbreviation

ALL: Acute Lymphoblastic Leukemia / Lymphocytic; AML: Acute Myeloid / Myelogenous Leukemia; CLL: Chronic Lymphocytic Leukemia;ML: Chronic Myeloid / Myelogenous Leukemia; WBC: White Blood Cell;CBC: Cell Blood Count; EPO: Erythropoietin;BM: Bone Marrow Biopsy; FISH: Fluorescence In Situ Hybridization; H&E: Hematoxylin And Eosin; WHO: World Health Organization; PDGFRA: Platelet-Derived Growth Factor Receptor A; DGFRB: Platelet-Derived Growth Factor Receptor Beta (Pdgfrβ); FGFRA: Fibroblast Growth Factor Receptor A; MD: Myelodysplastic Syndrome; MPN: Myeloproliferative Neoplasm; BCR: Breakpoint Cluster Region Protein; ABL-1: Abelson Murine Leukemia Viral Oncogene Homolog 1; EBV: Epstein Barr Virus; DLBCL: Diffuse Large B-Cell Lymphoma; ALK: Anaplastic Lymphoma Kinase; JAK2: Janus Activated Kinase; JAK2-V617F: Mutation Analysis Of Granulocytes And Platelets Of Patients With Chronic Myeloproliferative Disorder; FAB: French – American British; RARS: Refractory Anemia Ring Sideroblastic; RAEB: Refrectory Anemia Exce Blastic; CMML: Chronic Myelomonocytic Leukemia; RA: Refractory Anemia; RAEB: Refractory Anemia With Excess Blastic In Transformation; RCC: Refractory Cytopenia Of Childhood; PB: Perfiral Blood; Mds-U: Myelodysplastic Syndrome Unclassified; RUN1-RUNXT1: Runt-Related Transcription Factor / (RUNX1); JMML: Juvenile Myelomonocytic Leukemia; PML-RARA: Promyelocytic Leukemia/Retinoic Acid Receptor Alpha; CBFB: Core-Binding Factor Subunit Beta; MLL: Major League Lacrosse

References

1. Silberstein LE, Anastasi J. Hematology: Basic Principles and Practice E-Book: Basic Principles and Practice: Elsevier Health Sciences. 2017.
2. Organization WH. International classification of diseases for oncology (ICD-O) 3rd edition, 1st revision. 2013.
3. WHO: The Global Cancer Observatory. 2019.
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer J Clinicians/2018; 68: 394-424.
5. Health TMO. Palestinian ministry of health annual report. 2017.
6. Busjan R, Hasenkamp J, Schmalz G, Haak R, Trümper L, Ziebolz D. Oral health status in adult patients with newly diagnosed acute leukemia. Clinical oral investigate. 2018; 22: 411-418.
7. Mughal TI, Mughal T, Goldman J, Goldman JM, Mughal ST, Mughal S. Understanding leukemias, lymphomas and myelomas: CRC Press; 2009.
8. Ahmad S, Tandon N, Tiwari N, Mehdi SR, Zaidi N, Zaidi ZH. Frequency of different types of leukemia in bone marrow-study at a tertiary care center, lucknow. J Advan Medicine Medical Res; 2016: 1-7.
9. Swerdlow SH. WHO classification of tumours of haematopoietic and lymphoid tissues. WHO classification of tumours. 2008; 22008: 439.
10. Cecil RLF, Goldman L, Schafer AI. Goldman's cecil medicine, expert consult premium edition--enhanced online features and print, Health Sciences; 2012.
11. Janeway Jr CA, Travers P, Walport M, Shlomchik MJ. The components of the immune system. In: Immunobiology: The Immune System in Health and Disease 5th edition. edn. Garland Science; 2001.
12. Wikipedia: Leukemia. Wikipedia, the free encyclopedia 2019.
13. Ntziachristos P, Mullenders J, Trimarchi T, Aifantis I. Mechanisms of epigenetic regulation of leukemia onset and progression. Advance Immunol. 2013; 1-38.
14. Understanding Leukemia.
15. Howlader NNA, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, et al. SEER Cancer Statistics Review. In: 1975-2016.

based on November 2018 SEER data submission , posted to the SEER web site. 2019.

16. Thomas DA, Kantarjian HM, Jorgensen JL, Faderl S, Jabbour E, Konopleva M, et al. Outcomes continue to be favorable for de novo Philadelphia chromosome negative B-lymphoblastic leukemia (ALL) after therapy with hyper-CVAD (with or without rituximab) regimen. In Am Soc Hematology; 2012.
17. Advani AS. New immune strategies for the treatment of acute lymphoblastic leukemia: antibodies and chimeric antigen receptors. ASH Education Program Book. 2013; 2013: 131-137.
18. Hoelzer D, Huettmann A, Kaul F, Irmer S, Jaekel N, Mohren M, et al. Immunochemotherapy with rituximab improves molecular CR rate and outcome in CD20+ B-lineage standard and high risk patients; results of 263 CD20+ patients studied prospectively in GMALL study 07/2003. In Am Soc Hematology. 2010.
19. Zhao Y, Huang H, Wei G. Novel agents and biomarkers for acute lymphoid leukemia. J Hematol Oncol. 2013; 6: 40.
20. Lancet J, Gojo I, Burton M, Quinn M, Tighe S, Kersey K, Zhong Z, et al. Phase I study of the heat shock protein 90 inhibitor alvespimycin (KOS-1022, 17-DMAG) administered intravenously twice weekly to patients with acute myeloid leukemia. Leukemia. 2010; 24: 699.
21. Fresco P, Borges F, Marques M, Diniz C. The anticancer properties of dietary polyphenols and its relation with apoptosis. Current Pharmaceutical Design. 2010; 16: 114-134.
22. Huang WY, Cai YZ, Zhang Y. Natural phenolic compounds from medicinal herbs and dietary plants: potential use for cancer prevention. Nutrition Cancer; 2009; 62: 1-20.
23. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA: A Cancer J Clinicians. 2013; 63: 11-30.
24. Raghavan D, Ahluwalia MS, Blanke CD, Brown J, Kim ES, Reaman GH, et al. Textbook of uncommon cancer: John Wiley & Sons; 2017.
25. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. CA: A Cancer J Clinicians. 2014; 64: 9-29.
26. Garcia- Manero G. Myelodysplastic syndromes: 2014 update on diagnosis, risk- stratification, and management. Am J Hematol. 2014; 89: 97-108.
27. Cyopick P, Culliton R, Brockhausen I, Sutherland DR, Mills GB, Baker M. Role of aberrant sialylation of chronic myeloid leukemia granulocytes on binding and signal transduction by chemotactic peptides and colony stimulating factors. Leukemia lymphoma. 1993; 11: 79-90.
28. Den Boer ML, van Slegtenhorst M, De Menezes RX, Cheok MH, Buijs-Gladdines JG, Peters ST, et al. A subtype of childhood acute lymphoblastic leukaemia with poor treatment outcome: a genome-wide classification study. The lancet Oncology. 2009; 10: 125-134.
29. Madi KH. Annual health report for 2018. In. Gaza strip: The Ministry of Health, centers of information system Gaza. 2019; 64.
30. Madi KH. Annual mortality report for 2018. In. Gaza strip: The Ministry of Health, centers of information system Gaza. 2019; 22.
31. Huang X, Cortes J, Kantarjian H. Estimations of the increasing prevalence and plateau prevalence of chronic myeloid leukemia in the era of tyrosine kinase inhibitor therapy. Cancer. 2012; 118: 3123-3127.
32. Rathee R, Vashist M, Kumar A, Singh S. Incidence of acute and chronic forms of leukemia in haryana. Int J Pharmacy Pharmaceutical Sci. 2014; 6.
33. Jung KW, Won YJ, Oh CM, Kong HJ, Lee DH, Lee KH. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2014. Cancer Res Treatment: Official J Korean Cancer Assoc. 2017; 49: 292.