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OPEN ACCESS JOURNAL ISSN: 2148-6832

MSD Medical Science and Discovery
2020; 7(5):501-4

Research Article Doi: 10.36472/msd.v7i5.381

Evaluation of seasonal changes in the diagnosis of acute leukemia in Turkey

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Abstract

Objective: The etiology of acute leukemia (AL) has been under investigation for decades but the exact cause is still unknown. There are studies suggesting that infection plays a critical role in the development of AL in conjunction with other risk factors. In some studies, it has been shown that the incidence of AL increases after influenza endemics. This shows that viruses may play a role in the etiology. The theory that viruses might have a role in the etiopathogenesis created the idea that AL frequency may peak during some specific months; therefore, in this study, we aimed to research the relationship between AL diagnosis frequency and seasons in Turkey.

Method: The 186 patients who were diagnosed with de novo acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL) diagnosis at our center were included in the study.

Results: The frequency of ALL diagnoses were as follows: 25 (34.3%) in winter, 19 (26%) in spring, 15 (20.5%) in autumn, and 14 (19.2%) in summer. The frequency of AML diagnose was as follows: 24 (21.2%) in winter, 30 (26.6%) in spring, 27 (23.8%) in autumn and 32 (28.4%) in summer. In our study, we did not find a statistically significant relationship between AL diagnosis frequency and seasons.

Conclusion: According to our literature review, there are two studies including our study, searching for a relationship between AL diagnosis frequency and seasons in Turkey. Neither of the studies found a relationship between AL and seasons. According to our analysis the numbers of the patient in studies are limited; therefore the studies with high number of patients are needed to find out a relation between seasons and diagnosis time of AL.

Keywords: Acute leukemia, seasonality, acute myeloid leukemia, acute lymphoblastic leukemia

Introduction

Acute leukemias (AL) are hematological malignancies characterized by the abnormal proliferation of the blasts caused by hematopoietic myeloid or lymphoid precursors or both. They become symptomatic in a short time due to their aggressive nature. The most frequently seen AL type in adults is acute myeloid leukemia (AML) and it has an incidence of 5-8 /100.000 (1,2). On the other hand, acute lymphoblastic leukemia (ALL) has an incidence of 1.28/ 100.000 and it is less commonly observed in adults compared to AML (3).

The identification of causes and prevention from AL is the main goal. For this reason, the etiology of AL has been under investigation for decades, but the exact cause is still unknown. Benzene, radiation, toxic gases, chemicals, hereditary diseases, benign hematologic diseases, and viruses have been researched in the etiology of AL. Ionizing radiation and congenital genetic syndromes such as Down's, neurofibromatosis, Fanconi's anemia, and Bloom's Syndrome, all of them together explain less than 10% of cases (4). There are studies suggesting that infection plays a critical role in the development of AL in conjunction with other risk factors. However, until today no specific microorganism has been definitively associated with AL. On the other hand, in some studies, it has been shown that the incidence of AL increases after influenza endemics (5,6). This may show that viruses play a role in the etiology. In addition to these, there are studies indicating that the incidence of AL increases in some periods in a year.

Turkey is located between 36° - 42° north latitudes and 26° - 45° east longitudes. December, January, and February are winter months; March, April, and May are spring months; June, July, and August are summer months; September, October, and November are autumn months. In this study, we aimed to research the relationship between AL diagnosis frequency and season in Turkey.

Received 08-05-2019 **Accepted** 22-05-2020 **Available Online** 26-05-2020 **Published** 30-05-2020
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http://dx.doi.org/10.36472/msd.v7i5.381

Material and Methods

186 patients diagnosed with de novo AML and ALL at our center between December 2009 and March 2019 were included in the study. The data regarding the gender, age, leukemia type, and diagnosis date were retrospectively analyzed. The patients whose AL were diagnosed with the examination of the morphological findings of bone marrow aspirates and flow cytometry or immunohistochemical analysis, and who were over the age of 18 were included in the study. The patients diagnosed at a different center and whose diagnosis date could not be reached were not included in the study.

The statistical analyses were performed by using IBM SPSS Statistics v21 software. Descriptive statistics were applied for numerical data, and the Chi-square test was used for the evaluation of categorical data and comparisons among the groups.

Results

The AL patients included in the study consisted of 73 (39.2%) ALL and 113 (60.8%) AML patients. While the median age among ALL patients was 30 (range 16-58), it was 38 (range 18-64) among AML patients; the median age for all AL patients was 36 (range 16-64). 25 (34.2%) out of 73 ALL patients were female, and 48 (65.8%) of them were male whereas 39 (34.5%) out of 113 AML patients were female, and 74 (65.5%) of them were male.

The frequency of ALL diagnosis was the most common in December and for AML it was the most common in June, however, no statistically significant relationship was found between the frequency of AL diagnosis and months (Table 1).

The frequency of ALL diagnosis was the most common in winter and for AML it was the most common in spring, however, no statistically significant relationship was found between the frequency of AL diagnosis and seasons (Table 2).

Discussion

The pathogenesis of AL patients involves a complex chain of events that alter the proliferation and differentiation of hematopoietic precursor cells, chromosomal translocations, inversions, or point mutations (1-3). The factor triggering these events has not yet been clearly specified. It has been suspected that viruses could be one of the potential triggering factors associated with AL pathogenesis. The role of John Cunningham (JC) virus, Epstein-Barr virus, cytomegalovirus, and parvovirus B19 has been researched as an etiological factor in AL and parvovirus B19 has been found to play a potential role in the etiology of AL (7-11). The theory that viruses might have a role in the etiopathogenesis created the idea that AL frequency may peak during some specific months; therefore, studies have been conducted to search a relationship between AL diagnosis frequency and seasons in various countries.

In the study conducted by Gao et al., in Sweden, ALL diagnosis was the most common in winter although in Singapore and the United States of America a seasonal relationship in the diagnosis of ALL was not found (12). Similar to results in Sweden, in a previous study, it was reported that, in Finland, the diagnosis of ALL was the most common in winter (13). Contrary to the previous studies, Badrinath et al. indicated that ALL diagnosis was the most common in summer in England (14).

Table 1: The distribution of acute leukemia diagnosis times

Months	ALL (n, %)		AML (n, %)		p-value
January	9	(12.3%)	11	(9.7%)	
February	6	(8.2%)	6	(5.3%)	
March	8	(11%)	12	(10.6%)	
April	7	(9.6%)	11	(9.7%)	
May	4	(5.5%)	7	(6.2%)	
June	6	(8.2%)	13	(11.5%)	p=0,9
July	4	(5.5%)	9	(8%)	
August	4	(5.5%)	10	(8.8%)	
September	5	(6.8%)	8	(7.1%)	
October	2	(2.7%)	7	(6.2%)	
November	8	(11%)	12	(10.6%)	
December	10	(13.7%)	7	(6.2%)	
Total	73	(%100)	113	(%100)	

Table 2: The distribution of acute leukemia diagnosis times

Seasons	ALL (n, %)		AML (n, %)		p-value
Winter	25	(34.3%)	24	(21.2%)	
Spring	19	(26%)	30	(26.6%)	
Summer	14	(19.2%)	32	(24.8%)	p=0,2
Autumn	15	(20.5%)	27	(22.6%)	
Total	73	(%100)	113	(100%)	

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Ross et al. showed that ALL diagnosis is the most common in summer in the United States of America (15). In addition to the relationship between AL diagnosis frequency and season, the relationship between influenza epidemic and AL diagnosis was researched. It was shown that there were more ALL diagnosis during influenza epidemics. However, an increase in AML diagnosis was not found during the influenza epidemic. Eatough et al. found out that AML diagnosis is the most common in February and March in England (16). Calip et al. found that AML diagnosis was the most common in winter in various regions of the United States of America (17). In a study, it was reported that AML was diagnosed with the most common in September and October in Pakistan (18). Drapkin et al showed that the incidence of de novo AML increased between October and November (19). In a study including 833 AL patients in Mexico, no relationship between AL diagnosis frequency and the season was found (20). In the study conducted by Eren et al. in Istanbul, the frequency of acute leukemia diagnosis was the most common (13%) in August and the least in June (3.7%). In their study, all ALs were diagnosed with the following percentages with respect to seasons: 24.1% in winter, 24.7% in spring, 24.7% in summer, and 26.5% in autumn. They found no statistically significant relationship between the diagnosis of AL and seasons (21).

In our study, we found that ALL patients had their diagnoses in the following numbers, percentages and seasons: 25 (34.3%) in winter, 19 (26%) in spring, 15 (20.5%) in autumn, and 14 (19.2%) in summer. We also found that AML patients had their diagnoses in the following numbers, percentages and seasons: 24 (21.2%) in winter, 30 (26.6%) in spring, 27 (23.8%) in autumn, and 32 (28.4%) in summer. No relationship was observed between seasons and both ALL and AML.

Conclusion

In conclusion, among the studies examining the relationship between AL and seasons in various geographical regions of the world, some studies found a relationship between AL diagnosis frequency and seasons whereas some other did not reveal such a relationship. According to our literature review, there are two studies including our study, searching for a relationship between AL diagnosis frequency and seasons in Turkey. Neither of the studies found a relationship between AL and seasons. The number of the patients in this study is limited therefore studies with high number of patients are needed to find out a relation between seasons and diagnosis time of AL.

Acknowledgement, Funding: None.

Author's contributions: Design of the study: **T.N.Y,D.Ş.;** Literature search: **T.N.Y., M.B.;** Material preparation: **B.U.U. T.D.;** Data collection: **M.B., D.Ş.;** Analysis: **S.B.,J.Y.;** Preparation of article and revisions: **S.B., D.İ.,N.A.B., T.N.Y.;** Supervision and critical review**: M.K.Ç., M.S.D., F.A.**

Conflict of interest: The authors declare that they have no conflict of interest.

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