



# EPIDEMIOLOGY OF HEMATOPOIETIC CANCERS IN NORTH OF IRAN: RESULTS OF MAZANDARAN POPULATION-BASED CANCER REGISTRY

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**Abstract – Objective:** Hematopoietic malignancies include leukemias, lymphomas, plasma cell tumors, myelodysplastic syndromes, and malignant mastocytosis. There are very rare population-based epidemiological studies in hematopoietic cancers in Iran. The aim of this study was to describe the epidemiology of hematopoietic cancers in the north of Iran.

**Patients and Methods:** This longitudinal study was carried out on cancer incidence data of Mazandaran Population-based Cancer Registry (MazPCR), which is responsible for recording cancer cases in the population of all counties of Mazandaran province (except Babol, which is covered by the Babol University of Medical Science) in 2014. We used SPSS 16 (SPSS Inc., Chicago, IL, USA) for statistical analysis. Chi-Square test was used and *p*-values < than 0.05 were considered statistically significant.

**Results:** The Age-Standardized incidence Rates (ASRs) of leukemia were 8.2 and 5.4 per 100,000 in men and women, respectively. The ASRs of lymphoma among men and women were 7.1 and 3.2 and the ASRs of multiple myeloma were 1.7 for men and 1.8 for women. The ASRs of lymphoma and multiple myeloma in urban areas were higher than rural, while the ASR of leukemia in rural areas was higher.

**Conclusions:** The ASRs of leukemia and lymphoma were higher in males and the ASR of multiple myeloma was higher in females in this study. The ASRs of leukemia and Hodgkin's lymphoma in the MazPCR coverage area were higher than estimated ASRs in the world and Iran, while ASRs of Non-Hodgkin's lymphoma were lower than those estimated for the world and Iran.

**KEYWORDS:** Epidemiology, Leukemia, Lymphoma, Multiple myeloma, Iran.

## INTRODUCTION

Hematopoietic malignancies, a heterogeneous group of conditions characterized by the malignant growth of blood cells<sup>1</sup>, include leukemias, lymphomas, plasma cell tumors, myelodysplastic syndromes and malignant mastocytosis<sup>1-3</sup>. The classification of lymphomas and leukemias has become blurred in recent years<sup>4</sup>. Leukemias are

classified in four major subtypes, including Acute Lymphoblastic Leukemia (ALL), Chronic Lymphoblastic Leukemia (CLL), Acute Myeloid Leukemia (AML), and Chronic Myeloid Leukemia (CML)<sup>5,6</sup>. There are two types of lymphomas: Hodgkin and Non-Hodgkin; the latter has a higher global incidence than the first<sup>2</sup>. Multiple myeloma is a rare malignancy of plasma cells<sup>7,8</sup> and the second most frequent hematological malignancy



among other plasma cell dyscrasias<sup>8</sup> with a high mortality rate<sup>7</sup>. As stated in GLOBOCAN 2012, about 14.1 million new cancer cases were occurred all over the world, of which, 2.5%, 0.5%, 2.7% and 0.8% of the total were Leukemia, Hodgkin's lymphoma, Non-Hodgkin's lymphoma and multiple myeloma, respectively<sup>9</sup>. The incidence of hematopoietic cancers is low among developing countries<sup>2</sup>. Age-Standardized Incidence Rates (ASRs) of leukemia in men and women were 5.6 and 3.9 worldwide<sup>9</sup>, and 6.4 and 4.8 in Iran, respectively<sup>10</sup>. The ASRs of Non-Hodgkin's lymphoma were higher (6.0 among male and 4.1 among female) than Hodgkin's lymphoma (1.1 among male and 0.7 among female)<sup>9</sup>. The lowest rates of both kinds of lymphoma are in Asia<sup>9,11,12</sup>. According to Iran's latest report, the ASRs of Hodgkin's lymphoma were 1.5 and 1.1 among men and women, respectively. Also the ASRs of Non-Hodgkin's lymphoma were reported 4.5 and 3.1 for male and female, respectively<sup>10</sup>. The epidemiology of multiple myeloma is similar to leukemia<sup>5</sup>. Based on GLOBOCAN 2012, global ASRs of multiple myeloma were 1.7 in men and 1.2 in women<sup>9</sup>. These rates were 1.3 and 1.1 for men and women in Iran, respectively<sup>10</sup>. The incidence of cancer varies in different regions of Iran<sup>13</sup>. However, very rare population-based epidemiological studies have analyzed the incidence of hematopoietic cancers<sup>5,14,15</sup>. Therefore, this investigation was conducted to describe the epidemiology of Leukemia, Lymphoma and Multiple Myeloma in Mazandaran province (all counties except Babol, which is covered by the Babol University of Medical Science), north of Iran, which is covered by Mazandaran University of Medical Sciences (MazUMS).

## MATERIALS AND METHODS

This longitudinal study was carried out on data of cancer incidence in 2014. The studied population included all new cases of leukemia, lymphoma and multiple myeloma in 2,311,432 people covered by Mazandaran Population-based Cancer Registry (MazPCR). MazPCR collected information on newly diagnosed cancer cases from all public and private diagnostic and therapeutic centers in this area, including pathology and laboratory centers, hospitals, the only radiotherapy center and some specialist physicians' private offices. Moreover, information on cancer-related deaths was received from Death Registry Program of Health Deputy of MazUMS. Moreover, cancer cases were gathered from a national pharmaceutical database of the Ministry of Health and main insurance organizations of Mazandaran province. All patients

with malignancy were enrolled and patients with unknown age or residual status were excluded. After removing duplicates, we selected cancer cases, according to the third edition of International Classification of Diseases for Oncology (ICD-O-3) as follows: topography code C42 for Leukemia and Multiple Myeloma and C77 for Lymphoma. Extra nodal lymphomas were not considered in this study. In addition, patients in all age groups (<14 years and older) were enrolled in the study. The ASR was calculated by the direct standardization method. The standard population in this study was the 2000 world standard population and expressed per 100,000 population. The protocol was approved by the Ethics Committee of MazUMS (Ethics Committee Approval Code: IR.MAZUMS.REC.95.2677). Confidentiality measures were used to ensure the preservation of anonymity of cancer cases.

## STATISTICAL ANALYSIS

We used SPSS standard statistical software (SPSS 16 Inc., Chicago, IL, USA) for the statistical analysis. Chi-Square test was used and *p*-values < than 0.05 were considered statistically significant.

## RESULTS

Totally, 4460 new cancer cases were registered in MazPCR in 2014, of which 187 (4.2%), 141 (3.2%), and 46 (1.0%) new cases were leukemia, lymphoma and multiple myeloma, respectively. 79.5% of cases were diagnosed by Pathology/Immunohistochemistry (IHC), 19.8% by Death Certificate Only (DCO) and 0.8% by paraclinical assessment. The mean (SD) of age in patients with Leukemia, Lymphoma and Multiple Myeloma were 52.4 (24.6), 50.6 (18.9) and 64.3 (14.6), respectively. The ASRs for leukemia were 8.2 and 5.4 per 100,000 among men and women, respectively. In lymphoma, the ASRs were 7.1 and 3.2 for men and women, respectively. In case of multiple myeloma, the ASRs were 1.7 for men and 1.8 for women. Table I shows the characteristics of patients with leukemia, lymphoma and multiple myeloma, registered by MazPCR (Table I). The ASR of leukemia was 5.0 and 5.2 in urban and rural areas, respectively. Furthermore, the ASR of lymphoma was calculated 4.2 in urban and 3.9 in rural areas, respectively. The ASR of multiple myeloma was also found in urban and rural areas, 1.7 and 1.5, respectively. Table II shows number, crude rate and ASR of leukemia, lymphoma and multiple myeloma among men and women by type of cancer and gender (Table II).

**TABLE 1.** Characteristics of patients with leukemia, lymphoma and multiple myeloma in population covered by MazUMS, Iran, 2014.

Variable	Leukemia		Lymphoma		Multiple Myeloma		Asymp. Sig. (2-sided)	
	No.	%	No.	%	No.	%		
Gender	Male	115	61.5	96	68.1	23	50.0	0.08
	Female	72	38.5	45	31.9	23	50.0	
Place of residence	Urban	71	38.0	62	44.0	22	47.8	0.40
	Rural	69	37.0	47	33.3	18	39.1	
	Unknown	47	25.0	32	22.7	6	13.1	
Method of diagnosis	Pathology/ Cytology	127	67.9	129	91.5	41	89.1	0.00
	Death Certification Only (DCO)	58	31.0	11	7.8	5	10.9	
	Clinical/ Paraclinical Assessment	2	1.1	1	0.7	0	0	

## DISCUSSION

Our study was performed to examine the epidemiology of leukemia, lymphoma and multiple myeloma in MazPCR coverage area. This is the first study to investigate the incidence of hematopoietic cancers in the population covered by MazPCR. We found that the ASR of leukemia was 8.2 and 5.4 per 100,000 among men and women, respectively. These rates for men and women were reported 5.6 and 3.9 per 100,000 for the world and 6.9 and 4.7 per 100,000 for Iran, respectively<sup>9,16</sup>. The results of our study showed that the ASRs of leukemia in men and women in the population covered by MazPCR were less than the ASRs reported for Golestan province, which is neighboring Mazandaran province<sup>5</sup>. In addition, the incidence rate of leukemia was higher in males than females and it corresponds to those

observed in other studies<sup>5,15,17-19</sup>. The exact etiology of leukemia in adults is unknown, but it has been stated that various environmental and genetic factors such as ionizing radiation, certain chemicals, smoking and alcohol, some chemotherapy drugs and family history are involved in causing the disease. It seems that men are more vulnerable to these factors. Further studies can help to determine the risk factors of leukemia in this area. According to estimated cancer incidence in 2012, the ASRs of Hodgkin lymphoma in the world were 1.1 for men and 0.7 for women, and 1.6 and 1.1 for men and women in Iran, respectively<sup>9,16</sup>. The results of the present study showed that the ASRs of Hodgkin lymphoma for men and women were 2.3 and 1.1, respectively, which were higher than the estimated rates for Iran. On the other hand, the ASRs of Non-Hodgkin lymphoma were estimated 4.0 for

**TABLE 2.** Number of patients, crude rate and ASR of leukemia, lymphoma and multiple myeloma in population covered by MazUMS, Iran, 2014.

	Male			Female		
	No.	Crude rate	ASR	No.	Crude rate	ASR
<b>Lymphoma</b>	<b>96</b>	<b>10.5</b>	<b>7.1</b>	<b>45</b>	<b>10.8</b>	<b>3.2</b>
Hodgkin Lymphoma	31	3.4	2.3	15	3.5	1.1
Non-Hodgkin Lymphoma	54	6.0	4.0	26	6.1	1.9
Lymphoma, Nos	11	1.1	0.9	4	1.1	0.3
<b>Leukemia</b>	<b>115</b>	<b>13.9</b>	<b>8.2</b>	<b>72</b>	<b>14.4</b>	<b>5.4</b>
Lymphoid Leukemia	36	4.5	2.8	24	4.6	1.9
Myeloid Leukemia	40	5.1	2.7	28	5.2	2.2
Leukemia, Nos	39	4.4	2.7	20	4.5	1.3
<b>Multiple Myeloma</b>	<b>23</b>	<b>3.4</b>	<b>1.7</b>	<b>23</b>	<b>3.5</b>	<b>1.8</b>



men and 1.9 for women in the present study. These rates were lower than those reported for Iran (5.7 for men and 3.8 for women) as well as the world (6.0 for men and 4.1 for women)<sup>9,16</sup>. The difference between the ASRs in this study and the estimated ASRs for Iran needs further study. The ASRs of Non-Hodgkin lymphoma were higher than Hodgkin lymphoma in men and in the urban population. The ASRs of multiple myeloma were calculated 1.7 for men and 1.8 for women during this time period. These rates were reported for Iran 2.0 and 1.2 and for the world 1.7 and 1.2 for men and women, respectively<sup>9,16</sup>. So, the ASR of multiple myeloma in the men population covered by MazPCR was lower than those reported for the world. On the contrary, the ASR in women has been higher. Our study showed that ASR of multiple myeloma in urban areas was 1.7, which was lower than that of the neighboring province, Golestan. Whilst the ASR for rural areas was similar to the reported ASR of rural in that province (1.5 per 100000)<sup>5</sup>. The incidence rates of lymphoma and multiple myeloma were higher in urban than rural areas, in accordance with the study done in Southern Spain and Golestan province<sup>5,20</sup>. On the other hand, according to the Golestan Population Based Cancer Registry results, the incidence rate of leukemia in rural areas of Golestan province has been higher than that in urban areas<sup>5</sup>. The same result was obtained in this study. A limitation of this study was a high Death Certificate Only (DCO) rate, which indicates a degree of uncertainty in diagnosis. A higher rate of DCO in our registry is similar to results of first year activities of other registries in developing countries<sup>15</sup>. It is expected to decrease DCO rate with the regular cancer registration in the coming years.

## CONCLUSIONS

Further studies are needed to determine the environmental risk factors of leukemia, lymphoma and multiple myeloma and the survival rate of them in the studied population.

## CONFLICT OF INTEREST

The Authors declare that they have no conflict of interests

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