



## **Survival Rate of Patients with Acute Leukemia in Iran: A Systematic Review and Meta-analysis**

**Roohollah Askari<sup>1</sup>, Mohammad Ranjbar<sup>2</sup>, Mehran Nakhaeizadeh<sup>3</sup>, Shiva Sheikholeslami<sup>4\*</sup>, Sara Sepehrifar<sup>5</sup>, Morteza Adhami<sup>6</sup>, Zeinab Shabooni<sup>6</sup>**

<sup>1</sup> Department of Health Services Management, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup> Health Policy Research Center, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>3</sup> Department of Biostatistics and Epidemiology Faculty of Health, Kerman University of Medical Sciences Kerman Iran

<sup>4</sup> Department of Health care Management, International Campus, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>5</sup> Department of Biology Sciences in Sport, Sport Sciences Faculty, Shahid Bahonar University of Kerman, Kerman

<sup>6</sup> Shahid Bahonar Hospital, Kerman University of Medical Sciences, Kerman, Iran

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#### **\*Corresponding Author:**

Shiva Sheikholeslami  
International Campus of  
ShahidSadoughi University of  
Medical Sciences, Bafq  
Ancient Road, Yazd, Iran.

#### **Email:**

shiva.sh.eslami@gmail.com

#### **Tel:**

+98-9131966771

### **ABSTRACT**

**Background:** Leukemia is the fifth most common cancer among both genders. The prevalence of this type of cancer has been increasing in Iran. According to the Iranian Cancer Registry System, leukemia is among the first four cancer cases in terms of causing mortality. Considering the importance of survival rate of patients with acute cancers in Iran, this study aimed to study survival of patients with acute adult leukemia in Iran systematically.

**Methods:** In this study, all articles on the survival rate of patients with acute leukemia were searched throughout the Google scholar PubMedScopus, of science, Cochrane, Magiran, Irandoc, SID websites. Our search included the articles published up to June 2017. Using the keywords of Iran, Leukemia, Survival rate, blood cancer, life expectancy and their compositions. The search process was completed by two researchers independently. Then, all the reviewed articles and theses that met our inclusion criteria were examined. The data were analyzed using a comprehensive meta-analysis software and by running the Cochran test.

**Results:** We investigated eight studies with a sample of 1219 people in our meta-analysis. The findings showed that the 1-year survival rate for adults with acute leukemia was 61 % and the 5-year survival rate was 48 %.

**Conclusion:** According to the research findings, the survival rate of patients with acute leukemia in Iran is the same as other countries.

**Key words:** Iran, Leukemia, Survival rate, meta-analysis, Systematic study .

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**S**tatement of the problem and necessity of the study:

Socio-economic development and living standards have changed the pattern of diseases from infectious diseases 1). Despite the recent decades, in which the infectious diseases were controlled, the incidence of non-infectious diseases has been increasing. Cancer is a widespread disease that does not belong to a specific time or place (2 and is considered as one of the most important health (3). A significant Percent age of resources is allocated to cancer in the health systems 4 Cancer, as a problem in the society threatens the human health in all ages and causes a lot of financial burden and loss 5).

According to statistics, the global burden of cancers is on the rise (2,7,6). It is predicted that the number of new infections increase from 10 million in 2000 to 15 million in 2020 and 60 % of new cases occur in the developing countries 7 Cancer is one of the main causes of mortality (8 and the second leading cause of death in the world. It is also the third cause of death in Iran after heart disease and accidents (2,8,9 One out of four deaths in the US and one of three deaths in Iran are due to cancer (10, 11). Annually 30,000 people die due to cancer in Iran and this number is predicted to reach 62000 by 2020 (9).

Leukemia or blood cancer is the fifth most common cancer in both genders. The prevalence of this type of cancer has been increasing and the highest rates belong to the provinces of Yazd, Khuzestan, Isfahan, and Kerman in Iran (9.) According to the World Health Organization's reports, leukemia is rising both in the world and in Iran. According to the statistics provided by the Cancer registration system in Iran, leukemia is among the first four cancer cases causing death in Iran 12) .Leukemia is one variety of malignant diseases of the human blood system in various clinical and pathological forms, which may lead to death in a short time. Sometimes it leads to definite treatment and sometimes leads to death despite treatment with bone marrow transplantation 13).

There are four subtypes of leukemia: Acute lymphoblastic leukemia, Acute myeloid leukemia,

Chronic lymphoblastic leukemia, and chronic myeloid leukemia 16, 15, 14). About 70 % of leukemia cases are acute leukemia. Although the incidence of leukemia is not high, many of these cancer cases lead to death in a short time 15).

The effective factors on prevalence of this cancer include lifestyle changes and increased exposure to carcinogenic agents, such as cigarette smoking and increasing longevity (9. Considering the pathogenic aspect, these factors are related to a wide range of exposures, as well as genetic, infectious, and environmental factors (14 The global rate of death from acute leukemia is approximately 74 % out of 300000 new cases annually (15).

The estimation of the patients' survival rate after diagnosis is one of the main indexes for assessing the treatment 17 The survival duration is calculated by subtracting the date of death from the date of receiving the first pathology (blood) report (18). Generally, the survival rate of 5 years is used as an index in evaluating the results of cancer therapy interventions. This index shows the survival of the number of people with certain cancer in the fifth year of the diagnosis (19). Survival rates in developing countries are lower than the developed countries 6

Factors affecting the survival of patients with acute leukemia include the diagnosis age, number of white blood cell, blood factors, and time duration up to complete treatment (15,13). An important goal of meta-analysis studies is to reduce the amount of discrepancies among the existing variables and to decrease the confidence interval by including research studies and increasing the volume of samples. The meta-analysis studies also use scattered studies to provide evidences for clinical decision-making 19).

Considering the importance of the survival rate of patients with acute cancer in Iran, this study aimed to investigate this issue comprehensively by conducting a systematic review.

## Materials and Methods



The aim of this study was to determine the survival rate of patients with acute leukemia in Iran. So, all the articles conducted on this subject were searched and reviewed using the external databases of Google scholar, web of science, PubMed, Scopus, Cochrane as well as the internal data bases of SID, Irandoc, Magiran, and IranMedex. The search included the studies published from March 20, 1996 up to June 21, 2017. The search strategy in this study included two components of the PICO strategy; population and outcome. The English keywords were "cancer, leukemia, acute, survival, Iran" and the Persian keywords included "cancer, leukemia, acute, survival, life span, Iran" (In Persian). We also used a combination of the keywords in our search using the terms and and/or. Furthermore, to increase the sensitivity of the search and to select a larger number of studies, two independent researchers studied the reference lists of the investigated articles manually and added any possibly new articles.

Then, we eliminated the repeated studies after studying the titles and removed the irrelevant studies followed by reviewing the articles' titles, abstracts, and full texts according to the inclusion and exclusion criteria. Finally, eight papers on the 1-and 5-year survival were selected and entered the quality assessment stage.

### Inclusion criteria

All studies assessed the survival of adults with acute blood cancer in Iran and were published up to 21 June of 2017 entered the study.

### Exclusion criteria

- Studies conducted in foreign countries.
- Studies that discussed about Blood cancer, but they did not examine the acute leukemia.

Studies that examined the survival rate of children with acute leukemia or chronic leukemia.

- Studies that did not contain the survival rates and were not comprehensive.

Studies which full texts were not accessible.

Quality evaluation using a 12-part researcher-made checklist: After selecting the related studies in terms of titles, abstracts, and contents, a checklist was prepared for assessing the quality of

the documents. The checklist included 12 items that investigated the aim, method, sample size, sampling method, data collection tools, variables' measurement status, the target group, and the status of analyses in the articles. Each article was scored according to these items. The minimum acceptable score for an article to enter the meta-analysis process was eight.

We reviewed all the final articles by a data collection form designed in Excel. This form contained the authors' names, the year of publish, year that the study was conducted, the study location, the sample size, and the 1- or 5-year survival duration of adult patients with acute blood cancer.

### Statistical analysis

In the present study, all analyses were conducted using Comprehensive Meta-Analysis 3.0 software. The survival rates of 1- or 5-year were investigated in each study. Homogeneity analysis was conducted and the difference between studies in meta-analysis was examined. The Cochran's Q homogeneity test (Q test) and a related metric, the I<sup>2</sup> were applied among the studies. In the case that the result was greater than 50 % and Cochran's Statistics was less than 0.05, the studies were not homogeneous. Therefore, the random effects models must be used because other fixed effect models did not have the required efficiency. It is necessary to mention that this study tried to comply with Helsinki declaration principles.

### Results

In this study, 322 papers were selected, studied, and evaluated. Finally 8 papers were entered into the meta-analysis; out of which 2 papers examined the survival rate of 1- and 5-years, 3 articles examined the survival rate of 1 year, and 3 papers examined the survival rate of 5 years (Figure 1).

Of the 8 studies, 4 were conducted in Tehran, 2 in Mashhad, 1 in Isfahan, and 1 in Zahedan (Table 1).

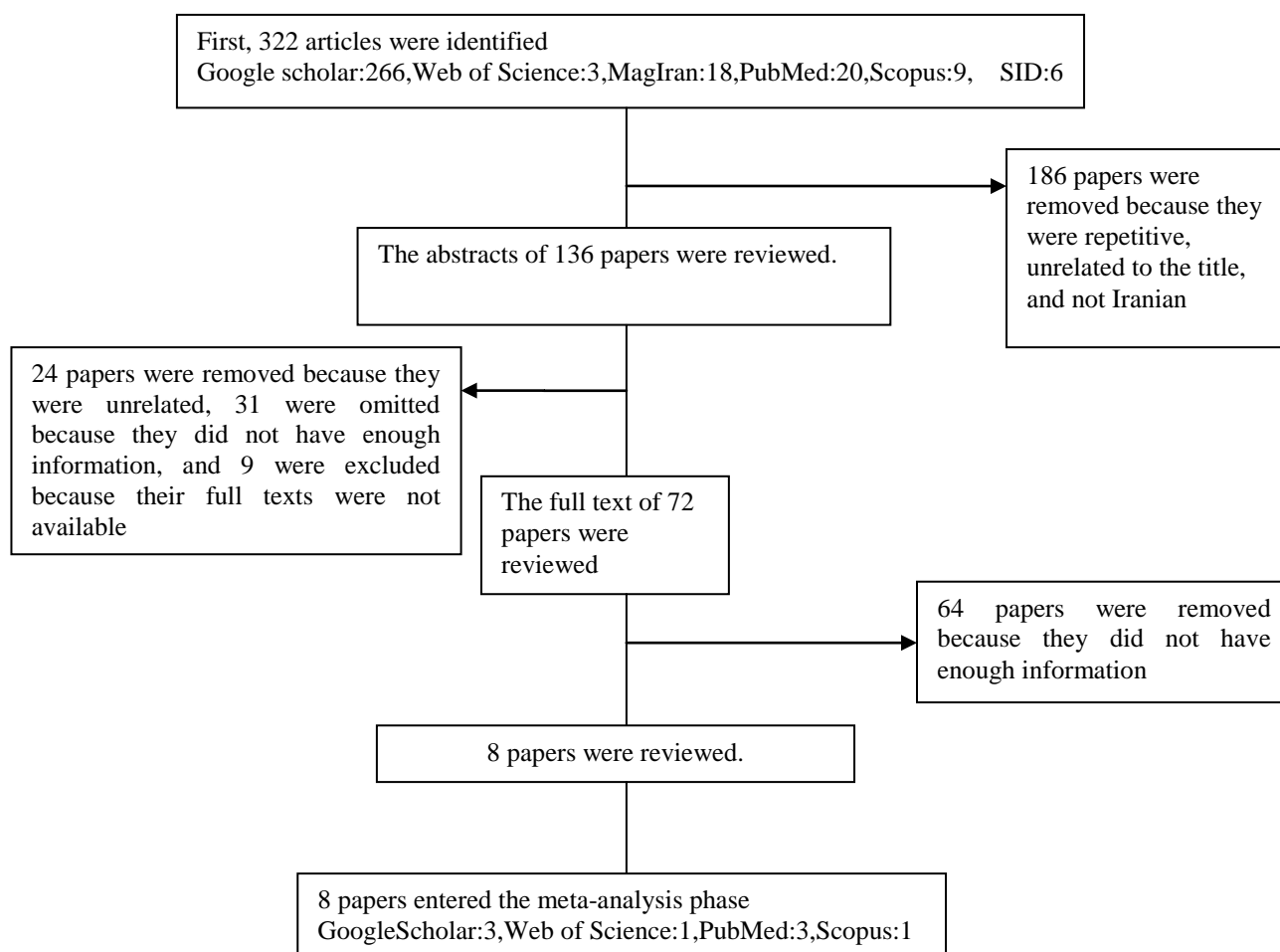
In this study, the total 1 - year survival rate of adults with acute leukemia in Iran was investigated as 61 % with the confidence interval of 95 % (0.67 to 0.54) (Figure 2).

The total 5- year survival rate of adults with acute leukemia in Iran was 48 % with a 95 % confidence interval. (0.5 to 0.46) (Figure 3).

Due to the lack of studies and required data on the survival rates of 2, 3, and 4 years in Iran, we did not include them in our study.

After conducting the homogeneity/heterogeneity test, the heterogeneity index ( $I^2$

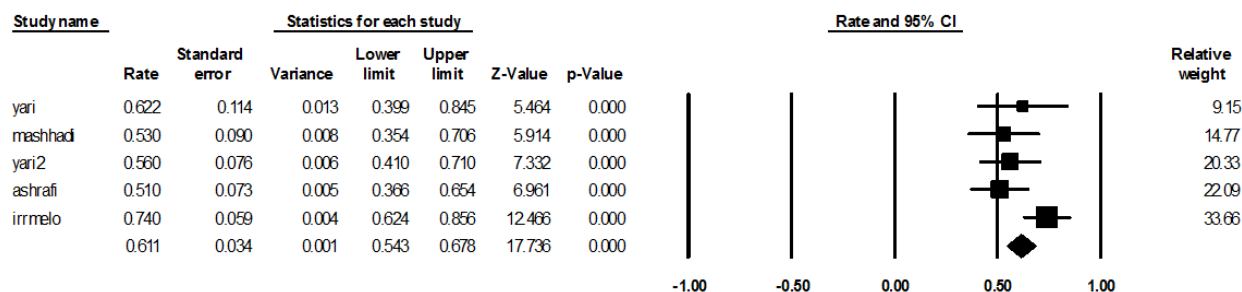
squared) was 49.3 % for the 1-year survival, which indicates homogeneity of studies under analysis. This index was 98.4 % for a 5-year survival rate indicating a high heterogeneity of the studies (Figures 4 and 5).



**Figure 1.** Article Selection Diagram

**Table 1.** Final studies under investigation

Authors' names	Publication year	Study year	Study location	Sample volume	5-year survival	4-year survival	3-year survival	2-year survival	1-year survival	The mean of survival	The median of survival	Confidence interval
Abolghasem Allahyari et al.	2016	2009-2015	Mashhad, Imam Reza Clinic	48	22.20 %				62.20 %			
Mohammad Ali Mashhadi et al.	2012	2004-2011	Zahedan, All-Ebne-Abitaleb Hospital	66					53 %		13 months	
Abolghasem Allahyari et al.	2016	2009-2015	Mashhad, Imam Reza Clinic	96	26.6 %				56 %			
Farzane Ashrafi et al.	2013	2002-2010	Isfahan, Seyyedoshohada Hospital	95					51 %		13 months	
Koorosh Sayemiri et al.	2008	1993-2007	Tehran, Shariati Hospital	206	52 %							47.3 - 56.7
Parvin Irimaloo et al.	2012	2001-2011	Tehran, Firoozgar and Rasool Akram Hospitals	210								
Koorosh Sayemiri et al.	2010	1993-2007	Tehran, Shariati Hospital	301	65 %							60.7 – 69.3
Ardesht Ghavami et al.	2011	1999-2010	Tehran	197	64.4 %							66.7

**Figure 2.** Forest diagram of one year survival

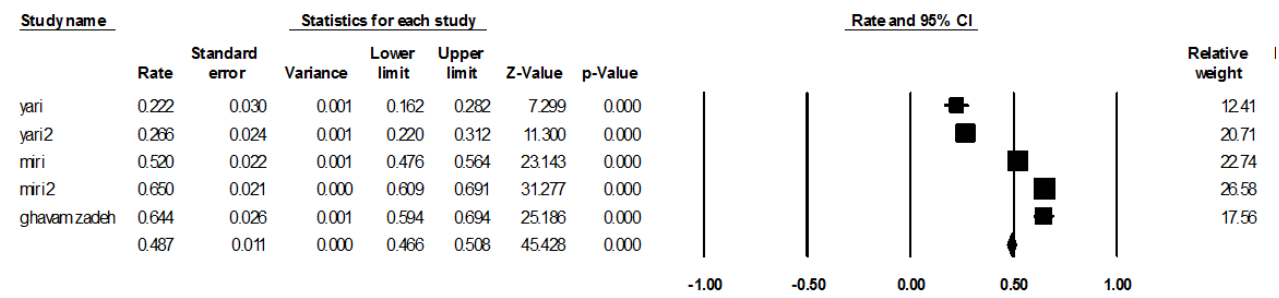


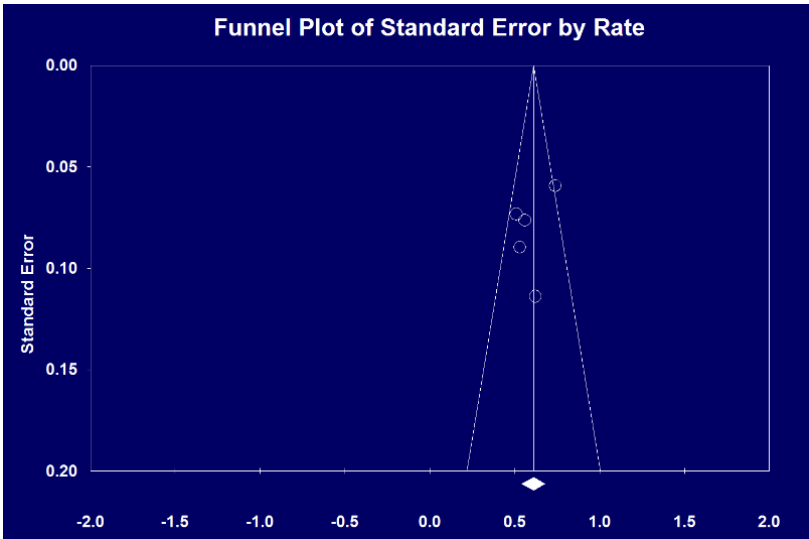
Figure 3. Tree diagram of 5 year longevity estimate

Model		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	5	0.611	0.034	0.001	0.543	0.678	17.736	0.000	7.895	4	0.096	49.334	0.006	0.009	0.000	0.078
Random	5	0.599	0.050	0.002	0.501	0.697	11.987	0.000								

Figure4: Homogeneity test of one year survival

Model		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	5	0.487	0.011	0.000	0.466	0.508	45.428	0.000	265.428	4	0.000	98.493	0.038	0.028	0.001	0.0
Random	5	0.461	0.088	0.008	0.289	0.633	5.241	0.000								

Figure 5. Homogeneity test of 5 year survival







## Discussion

According to the information of cancer registration system in Iran, leukemia is among the first four cancer cases in terms of mortality rate in Iran <sup>12</sup> Regarding the importance of the estimated survival rate of patients, which is one of the main indexes for assessing treatment <sup>17</sup> we conducted this study. In this systematic study, we investigated the survival rates of adults with acute leukemia in Iran comprehensively.

To the best of our knowledge, this is the first systematic and meta-analysis on the survival rate of adults with acute blood cancer in Iran. Various reports from various studies around the world should show different rates of survival for the patients with acute leukemia, including lymphoid and myeloid.

For example, in the study of Sankaranarayanan, 14 countries and 27 areas were compared in terms of cancer incidence in Africa, Asia, Caribbean, and Central America. It was concluded that in countries with more advanced health services, early diagnosis provided better care and clinical follow-up and consequently the survival rates of the patients were higher in these countries (20).

In the present study, the 1-year survival rate for patients with acute leukemia was 61 %. This rate in Turkey was 73.1 % and in Lampang, Thailand and Singapore was about 56 % <sup>20</sup> Furthermore, the 5-year survival of patients with leukemia was 48 % in this study. We found a lot of differences among countries of the world in this regard, which was due to the differences in their health systems.

The 5-year survival rate for leukemia patients in Shanghai, China was reported as 18.15 % in 2011, 66.7 % in Tianjin, and 41.8 % in Izmir, Turkey <sup>20</sup>. As we can see, there are many differences in the 5-year survival rates. Moreover, this rate was about 32 % in Singapore and 37 % in Thailand (20).

The strengths of this study included comprehensive investigations by two independent researchers, application of advanced search techniques, use of endnote software, and detailed

study of articles to enter this research. The weaknesses of this study included the scarce and inadequate studies on longevity rates of leukemia patients and the factors affecting their survival, especially the impact of different stages of the disease and treatment methods on the survival.

## Conclusion

In this study, the 1-year survival rate of adults with acute leukemia in Iran was 61 %.

The 5-year survival rate of adults with acute leukemia was 48 %, which is almost the same as other countries. Furthermore, the importance of the age of the diagnosis shows that sooner diagnosis of the disease leads to longer life periods. Regarding the inadequacy of studies in different regions of Iran, more comprehensive studies are needed for a more precise estimate of longevity rate and factors affecting it, in the whole country.

Therefore, more consideration should be given to examination, calculation, and implementation of methods to increase the survival rate of cancers, especially acute leukemia in Iran.

Code of Ethics: IR.SSU.SPH.REC.1396.158

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## Conflicts of Interest

The authors of this study did not have any conflicts of interests.

## Authors' contributions

Askari R and Ranjbar M designed research. Sheikholeslami Sh and Sepehrifar S and Adhami M did the searching. Sheikholeslami Sh conducted research. Nakhaeizadeh M analyzed data and performed meta analysis. Sheikholeslami Sh and Shabooni Z wrote the paper. Sheikholeslami SH had primary responsibility for final content. All authors read and approved the final manuscript.



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