# The Effect of the Chernobyl Disaster on the Occurrence of Adult Acute Leukemias in Turkey

## Çernobil Felaketinin Türkiye'deki Erişkin Yaş Akut Lösemi Üzerine Etkisi

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Geliş Tarihi/*Received:* 27.05.2008
Kabul Tarihi/*Accepted:* 07.10.2008

*A part of the data presented in this manuscript was presented in the XXVII. National Hematology Congress and IV. Leave After Education Course, İstanbul, 1999.*

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**ABSTRACT Objective:** The aim of this study was to investigate whether the occurrence of adulthood acute myelogenous leukemia (AML) and acute lymphocytic leukemia (ALL) had increased before and after the Chernobyl accident in the Hospital of the Hacettepe University Faculty of Medicine, one of the major tertiary care referral centers in Turkey. In addition, any increase in the number of patients with leukemia presenting from the Black Sea Region (BSR; the northern part of Turkey), which was presumed to be the most influenced region by ionizing radiation before and after the disaster was also assessed. **Material and Methods:** The study consisted of patients diagnosed with AML and ALL and hospitalized between 1976 and 1994 years. This interval was divided into two periods according to the date of the Chernobyl accident. The period before the Chernobyl accident (BCP) covered between 1976 and 1985 and the period after the Chernobyl accident (ACP) covered between 1989 and 1994. The hospital registration forms were retrospectively analyzed to determine the number of patients with AML and ALL in those periods. In addition, patient files were reviewed to record the place of residency, which was not included in the registration records. **Results:** The numbers of patients with AML and ALL in BCP and ACP were 194 and 380, and 96 and 151, respectively. There was a linear upward trend for each disease in BCP. These trends disappeared for each disease in ACP. The distribution of patients with AML and ALL in BCP was significantly different when compared to the distribution in ACP ($p< 0.00$ and $p= 0.005$, respectively). After eliminating the trends by difference transformations, the differences between the periods disappeared for each disease ($p= 0.92$ and $p= 0.60$, respectively). The number of AML and ALL patients presenting from the BSR did not show a significant difference between the BCP and ACP ($p= 0.74$ and $p= 0.36$, respectively). **Conclusion:** The disappearance of the significant differences between periods after the elimination of the trends in BCP for each disease indicate that the differences were due to the significant linear increases in the numbers of patients with each disease in BCP and not to periodical changes. In addition, the number of patients presenting from the BSR after the Chernobyl disaster was not significantly different.

**Key Words:** Radiation, ionizing; leukemia; epidemiology

**ÖZET Amaç:** Bu çalışmanın amacı, Çernobil kazası öncesi ve sonrasında Türkiye'de en önemli üçüncü derecede referans merkezlerinden biri olan Hacettepe Üniversitesi Tıp Fakültesi Hastanelerine başvuran erişkin akut miyeloid lösemi (AML) ve akut lenfoblastik lösemi (ALL) olgularında artış olup olmadığını araştırmaktır. Ayrıca, kazadan önce ve sonra iyonize radyasyondan en çok etkilendiği kabul edilen Karadeniz Bölgesi'nden başvuran lösemik hastaların sayısında artış olup olmadığı da incelenmiştir. **Gereç ve Yöntemler:** Bu çalışma, 1976-1994 yılları arasında AML ve ALL tanısı alınıp hastaneye yatırılan hastalardan oluşmaktadır. Çernobil kazasına göre bu aralık 2 döneme ayrıldı. Kazadan önceki dönem (ÇÖD) 1976-1985 yıllarını, kazadan sonraki dönem (ÇSD) ise 1989-1994 yıllarını kapsamaktadır. Her iki dönemdeki hastaların sayısına ulaşmak için hastane arşivinin kayıt formları incelendi. Kayıt formlarında hastaların yaşadıkları yer kayıtlı olmadığı için, ikinci aşamada, hastaların dosyaları incelendi. **Bulgular:** Hastane arşivinin kabul formlarına göre, ÇÖD ve ÇSD'deki AML ve ALL hastaların sayısı sırasıyla 194 ve 380 ile 96 ve 151 idi. Her iki hastalık grubunda ÇÖD'de doğrusal bir artış eğilimi saptandı. Bu eğilimin ÇSD'de kaybolduğu görüldü. ÇÖD'deki AML ve ALL hastalarının dağılımı ÇSD'kilerle kıyasladığında, dönemler arasında anlamlı bir fark gözlendi (sırasıyla $p<0.001$ ve $p=0.005$). Farklılık transformasyonu yapılarak eğilimler ortadan kaldırıldıktan sonra, her iki hastalık grubunda da bu farklılığın ortadan kaybolduğu görüldü (sırasıyla $p= 0.92$ ve $p= 0.60$). ÇÖD ve ÇSD'de Karadeniz Bölgesi'nden başvuran AML ve ALL hastalarının sayıları arasında fark bulunmadı (sırasıyla $p= 0.74$ ve $p= 0.36$). **Sonuç:** ÇÖD'de her iki hastalık grubunda artış eğilimleri ortadan kaldırıldıktan sonra, dönemler arasındaki istatistiksel farklılığın kaybolması, bu farklılıkların, ÇÖD'de her iki hastalık grubundaki dönemsel değişime değil, anlamlı lineer artışa bağlı olduğuna işaret etmektedir. Ayrıca, Çernobil felaketinden sonra, Karadeniz Bölgesi'nden başvuran hastaların oranlarında fark saptanmamıştır.

**Anahtar Kelimeler:** Radyasyon, iyonize; lösemi; epidemiyoloji



**Turkiye Klinikleri J Med Sci 2009;29(2):388-94**

The accident, which occurred on April 26th, 1986 in the reactor 4 of the Chernobyl nuclear power plant in the Ukraine, released considerable amounts of radioactive substances into the environment. Most exposure was due to radioactive iodine and Caesium (Cs). Iodine, which has a half-life of about 8 days, was only important in the first weeks following the accident while the contribution of Cs to exposure, particularly $^{137}Cs$, which has a half-life of 30 years, will continue to be important for many years.[1] These radionuclides may enter the human body via polluted water and food reservoirs in the nature. After the accident, the radioactivity doses received by adults in Europe have been determined by scientific studies. Accordingly, the adult dose in areas of low contamination such as Portugal and Spain were 0.2 μSv, but it reached over 200 μSv in highly contaminated countries such as Ukraine, Belarus, the Russian Federation, Finland, Sweden, and Germany.[1,2]

Following the accident, many studies focused on various possible health consequences of the accident, ranging from changes in birth rates to adult cancer were run in highly contaminated regions and the remaining European countries. Most of them focused on most contaminated regions surrounding the damaged reactor in Ukraine, Belarus and the Russian Federation, followed by other European countries. Due to large clouds loaded with radioactive isotopes, Turkey, especially the northern parts [Black Sea Region (BSR)], was also influenced by ionizing radiation.[1-4] The adult dose in Turkey was 190 μSv.[2,5,6]

The clearest effect seen to date has been the dramatic increase in thyroid cancer in children. The evidence for an increased incidence of leukemia is less clear, but there are indications of increased leukemia incidence in Russian clean-up workers.[7-9] Most of the previous studies focused on childhood cancers, especially leukemia and there were limited studies including adulthood acute leukemias.[10-12] In this retrospective study, we aimed to search if there was any increased occurrence of adulthood acute myelogenous leukemia (AML) and acute lymphocytic leukemia (ALL) before and after the Chernobyl accident in the Hospitals of Hacettepe University Faculty of Medicine in Ankara, one of the major tertiary care referral centers in Turkey and located in the Middle Anatolian Region of Turkey. Moreover, we also tried to assess if there was any increase in the number of patients with leukemia presenting from the BSR (the Northern part of Turkey) before and after the disaster.

## MATERIAL AND METHODS

This study consisted of patients who were diagnosed with AML and ALL and were hospitalized in the Hacettepe University Hospital between 1976 and 1994. According to the date of the Chernobyl accident, this interval was divided into two periods; the period before the accident (BCP) and the period after the accident (ACP). BCP covered between 1976 and 1985. Because the effects of radiation can be observed as early as 2-5 years after exposure, 2 years after the accident was excluded.[2] Accordingly, ACP covered between 1989 and 1994.

The hospital registration forms were retrospectively analyzed to determine the number of patients with AML and ALL in those periods. In addition, patient files were investigated to record the place of residency, which was not included in the registration records.

### STATISTICAL ANALYSIS

SPSS 13.0 (SPSS Inc., Chicago, IL) computer program was used for the statistical analyses. Time series analysis (exponential smoothing method) was used to estimate trends. Trend types were tested by regression analysis (curve estimation test). To compare the distribution of patients for each disease between the periods, ARIMA model was used. Difference transformation was used to eliminate the trends. Chi-square test was used to evaluate the ratios of patients from BSR and from other regions. A P value below 0.05 was considered statistically significant.

## RESULTS

According to the registration forms of the hospital archives 194 patients with AML and 96 ALL in the BCP, and 380 AML and 151 ALL in the ACP were diagnosed and hospitalized (Table 1).

**TABLE 1:** The number of patients with AML and ALL according to the registration forms in the hospital archives with respect to years.

| Years | Number of patients with AML | Number of patients with ALL |
|---|---|---|
| 1976 | 6 | 7 |
| 1977 | 15 | 6 |
| 1978 | 14 | 2 |
| 1979 | 10 | 8 |
| 1980 | 17 | 4 |
| 1981 | 11 | 10 |
| 1982 | 26 | 13 |
| 1983 | 30 | 7 |
| 1984 | 33 | 16 |
| 1985 | 32 | 23 |
| 1986 | 60 | 19 |
| 1987 | 68 | 17 |
| 1988 | 63 | 25 |
| 1989 | 62 | 22 |
| 1990 | 65 | 30 |
| 1991 | 75 | 36 |
| 1992 | 70 | 22 |
| 1993 | 51 | 18 |
| 1994 | 57 | 23 |

AML: Acute myelogenous leukemia; ALL: Acute lymphocytic leukemia.

The distributions of the patients according to the periods were shown in Figures 1a, 1b, 2a and 2b. There was a global upward trend for each disease in BCP. This trend disappeared for each disease in ACP. The upward trend was linear in BCP ($p_{AML}$= 0.001 and $p_{ALL}$= 0.01). When distributions of the patients with AML and ALL in BCP were compared to those in ACP, the difference was significant (p< 0.001 and p= 0.005, respectively). These differences may be due to the trends in BCP. After eliminating the trends by difference transformations, these differences between periods disappeared for each disease (p< 0.92 and p= 0.60, respectively).

Since the hospital registration forms did not include the data for place of residence, patient files were also reviewed and the files of 375 (65.3 %) AML and 139 (56.2 %) ALL patient were studied (Tables 2 and 3). There was no statistically significant difference in the number of AML and ALL patients presenting from the BSR between the BCP and ACP (p= 0.74 and p= 0.36, respectively).

## DISCUSSION

Ionizing radiation is among the most studied and best-quantified carcinogenic agents in our environment. Although the risk of cancer can be increased by exposure in virtually every tissue of the human body, leukemia, excluding chronic lymphocytic leukemia (CLL), is among the cancers most strongly related to radiation exposure, and numerous studies have shown that radiation-related increases in the risk of this disease could be observed as early as 2-5 years after exposure.[2,13,14]

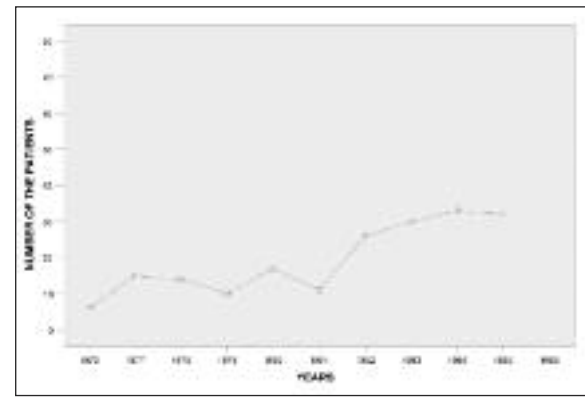

**FIGURE 1A:** Annual distribution of patients with acute myelogenous leukemia before Chernobyl accident.

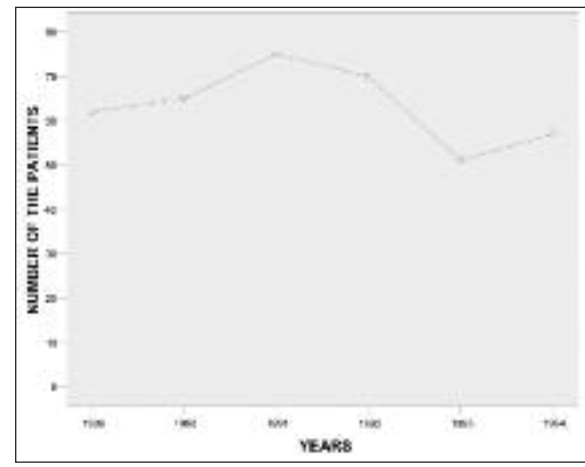


**FIGURE 1B:** Annual distribution of patients with acute myelogenous leukemia after Chernobyl accident.

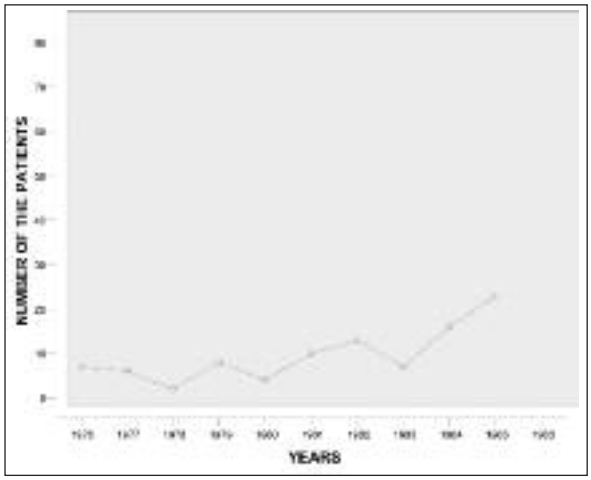


**FIGURE 2A:** Annual distribution of patients with acute lymphocytic leukemia before Chernobyl accident.

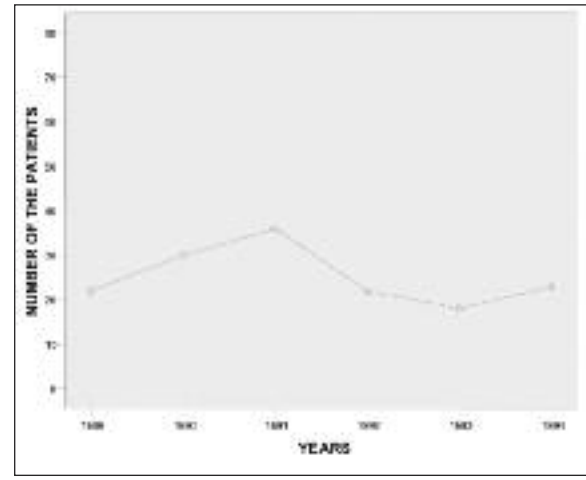


**FIGURE 2B:** AAnnual distribution of patients with acute lymphocytic leukemia after Chernobyl accident.

The nuclear reactor fire in Chernobyl continued for 10 days and an intense contamination with radioactive nuclides took place during this period. After the Chernobyl accident, many studies were run mostly in highly contaminated regions and the remaining European countries. Some studies focused on the risks of leukemia among liquidators and breast cancer among young women in the most contaminated areas.[15,16] Excluding some studies from the most contaminated regions, no significant association has been found in any of the studies between public health and exposure from the Chernobyl accident.[17-19] An increase in the incidence of thyroid cancer has been observed among those exposed to radioactive iodines in childhood and adolescence in most contaminated regions.[20-24] Although a slightly more often than expected NHL and lung cancer in persons, who had participated in the cleanup activities in the Chernobyl area, and an increase in breast cancer incidence in Belarus and Ukraine were found, no significant increase in the incidence of solid cancers was seen.[8,9,16,25-29] Because radiation-related risks of solid cancers remain elevated throughout life, it is too early to evaluate the full radiological effect of the accident.[29-31]

Although an increase in infant leukemia in northern Greece and Belarus exposed in utero have been reported, these result have not been confirmed.[32-35] Hence, the association between leukemia and in utero exposure is still unclear.[30] The current evidence on the association between leukemia risk and exposure to radiation from the accident in childhood is limited and conclusion cannot be drawn about possible increases in childhood leukemia.[25,30,36-38] On the other hand, none of these studies is sufficiently sensitive to detect small changes in the incidence of rare diseases such as leukemia. A case-control study from Ukraine suggested a sig-

**TABLE 2:** The number of patients with acute myelogenous leukemia with respect to periods and regions.

| | Number of patients admitted from BSR | | Number of patients admitted from other regions | | Total |
|---|---|---|---|---|---|
| | n | % | n | % | n |
| BCP | 56 | (%31.6) | 121 | (%68.4) | 177 |
| ACP | 66 | (%33.7) | 132 | (%67.3) | 198 |
| General | 122 | (%32.5) | 253 | (%67.5) | 375 |

BCP, the period before the Chernobyl accident; ACP, the period after the Chernobyl accident; BSR, Black Sea Region.

**TABLE 3:** The number of patients with acute lymphocytic leukemia with respect to periods and regions.

| | Number of patients admitted from BSR | | Number of patients admitted from other regions | | Total |
|---|---|---|---|---|---|
| | n | % | n | % | n |
| BCP | 26 | (%31.7) | 56 | (%68.3) | 82 |
| ACP | 14 | (%24.5) | 43 | (%75.5) | 57 |
| General | 40 | (%28.7) | 99 | (%71.3) | 139 |

BCP, the period before the Chernobyl accident; ACP, the period after the Chernobyl accident; BSR, Black Sea Region.

nificant association between leukemia risk and radiation dose to bone marrow.[39] Apart from the dramatic increase in 'young thyroid cancer' incidence and some increase in leukemia and solid cancer in most exposed workers, there is no clearly demonstrated increase in the somatic diseases due to radiation.[40]

Although Turkey has also been affected by ionizing radiation from the accident, a few studies focused on child cancer have been run. An increase in acute leukemia and neural tube defects in children was reported in the studies from the northern part of Turkey, which was presumed to be more influenced by the nuclear catastrophe.[3,4,41,42]

Because we have not had high quality national cancer registration, which is one of the main problems for developing countries, we used the registration form of Hacettepe University Medicine Faculty Hospitals, which is the nearest third degree reference center to BSR. The first aim of our study was to determine whether or not there was any increase in the incidences of acute leukemia diagnosed and hospitalized in our institution between 1976 and 1994 years.

When the graphics were analyzed, there were global upward trends in each disease in BCP. But, these global upward trends in each disease were disappeared in ACP. The types of these upward trends in BCP were linear ($p_{AML}$= 0.001 and $p_{ALL}$= 0.01). Except NHL, the incidence rate of hematolymphopoietic malignancies are strikingly stable in most western countries, however, many factors such as increasing number of people in industrial area, improvement in health service may be responsible for increase in the incidences of these disease in developing countries. Those reasons may explain the increases in both diseases in BCP. When distributions of the patients with AML and ALL in BCP were compares to the distributions in ACP, there were significantly differences (p< 0.001 and p= 0.005, respectively). These differences may be due to the trends in BCP. After eliminating the trends by difference transformations, these differences between periods were disappeared in each disease (p= 0.92 and p= 0.60, respectively). These showed us that the differences were due to the upward trends in BCP, not due to periodical changes.

Because the registration form does not include the data about place of residence of the patients, at the second stage, the files of the patients with those diseases were studied to determine any significant changes in the numbers patients from BSR. In any patient groups, there were no significantly changes in the numbers of the patients admitted to our referral hospital from BSR and out of BSR between those periods (p > 0.05). Likewise, a previous study provided no convincing evidence of an increased risk of childhood leukemia as a result of exposure to Chernobyl radiation in Belarus, Russia, and Ukraine.[38] Excess of thyroid cancer cases, two unconfirmed diagnoses of leukemia cases, and the excess cases of brain tumors have been indicated in a study from Estonia and Latvia.[8,9] Increments in acute leukemia incidence in Donetsk region of Ukraine was attributed to radionuclide contamination after the Chernobyl accident of a region with initially unfriendly environment.[43] Increased incidence of total malignancies possibly related to the fallout from the Chernobyl accident is seen in Sweden.[44] Konogorov and coworkers estimated the radiation-induced risk of leukemia in 162,684 Chernobyl accident emergency workers using the data of the Russian National Medical and Dosimetric Registry.[27] Based on their data, the principal analysis included 41 leukemia cases that occurred more than 2 years after the first exposure to radiation. The relative risk estimates for leukemia, excluding CLL, were greater than the value for all leukemia and were greater than one. The estimated excess relative risk per Gy was greater for all emergency workers.[27] In the studies by Gluzman et al, the data on 218 consecutive cases of malignant diseases of hematopoietic and lymphoid tissues in Chernobyl clean-up workers diagnosed in 1996-2005 were given in comparison with the data of 2697 consecutive patients of general population of the same age group.[16,28] Myelodysplastic syndrome (MDS) percentage among patients of clean-up workers group tended to exceed MDS percentage in the group of patients representing the general population examined at the same period (4.58 vs.

3.70%).[28] Among 34 AML cases, leukemia was preceded by MDS in seven patients.[28]

## CONCLUSION

The disappearance of the statistically significant differences between periods after elimination of the trends in BCP for each disease show that the differences were due to the significant linear increases in the number of patients with each disease in BCP, not to periodical changes. In addition, there was no difference in the incidence of those diseases in the BSR after the Chernobyl disaster. On the other hand, the trends of changes in the cancer incidence over time and across different regions with various levels of radiation contamination should be monitored closely in order to better understand the late and exact mutagenic and teratogenic effects of especially low-dose radiation.

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