CHRONIC LYMPHOCYTIC LEUKEMIA AND OCCUPATIONAL RISK

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ABSTRACT

Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in adults. The incidence of CLL is about 3-4/100 000 inhabitants in European countries (25% of all leukemia). About 163 new patients with CLL are diagnosed in Bulgaria every year. The exact causes of the disease are unknown, such as family history is extremely rare. The aim of this work was to investigate occupational risk in patients with CLL. Material and Methods: Available literature for a period of five years was analyzed. The influence of risk factors in the work environment and the incidence of CLL were examined. For the same period was made characteristic of patients with CLL according to demographics and occupation which were registered in the Department of Hematology at the University Hospital - Stara Zagora. Results: Epidemiological studies were focused on the chemical and physical factors of the working environment. It was found an increased risk for CLL in exposed to benzene, chlorinated aromatic hydrocarbons, mineral oils, pesticides. Of all physical factors of the working environment, ionizing radiation and electro-magnetic fields were mostly studied. Data from our study showed that only 22 (42.3%) of registered patients with CLL (52) have noted occupation in their medical records. Work with pesticides were noted 40.9% of patients with CLL, while 18.2% - of exposure to toxic substances. Conclusion: The lack of data on occupational risk assessment for CLL in the country, showed the need for similar studies at regional and national level. The introduction of the electronic health record containing information about the occupation of patients and related conditions of employment is essential for occupational risk assessment and diseases.

Key words: pesticides, benzene, ionizing radiation, electro-magnetic fields.

INTRODUCTION

Chronic lymphocytic leukemia (CLL) is a monoclonal disorder characterized by a progressive accumulation of functionally incompetent lymphocytes (1). It is the most common type of leukemia in adults in western Europe, amounting to 25-30% of all cases. CLL is characterized by progressive, uncontrolled expansion of mature, but functionally incompetent lymphocytes and their accumulation in the blood, bone marrow, lymph nodes and spleen (Figure 1) (2, 4). Approximately 3 of every 100,000 people get sick from CLL, as the majority of patients were males (M/F sex ratio of at least 1.5 or higher) (2). About 163 new patients with CLL are diagnosed in Bulgaria every year. This cancer is found most often in older people and the median age of patients at diagnosis is 65 years (4). Some patients die rapidly, within 2-3 years of diagnosis, because of complications from CLL, but most patients live 5-10 years, survival ranging is from months to decades (1, 3). Malignant mononuclear cells in CLL have B-cell origin and most often resemble mature lymphocytes and only 2-5% of the patients had T-cell phenotype (5). Major progress has been made in identification of molecular and cellular markers that could predict disease progression in patients with chronic lymphocytic leukaemia (3). Some characteristic changes in CLL established by:

- flow cytometry CD5+, CD19+, CD20+, CD10+, CD23+ (ZAP70; CD38)
- cytogenetic analysis- t(11;14), t(11q:v); +12; del(11q); del(13q); del(17p)
- molecular - genetic analysis -mutational profile of immunoglobulin genes- IGHV.

The exact etiology causes of the disease are unknown (5). The importance of genetic factors in etiology of CLL is suggested by family and population studies, show that the
increase in the risk of illness of relatives is small and even sporadic (6, 7).

Environmental influences on the development of CLL is not fully understood due to the lack of data and the small count conducted similar studies.

Of all physical factors of the working environment, ionizing radiation and electromagnetic fields were mostly studied. Despite association between ionizing radiation and CLL is weak, epidemiologic findings are consistent with a hypothesis of elevated CLL mortality risk after a latency and morbidity period that spans several decades (8). There are various studies about the relationship between elektro-magnetic fields and CLL. Most of them support the hypothesis that occupational exposure to low frequency electromagnetic fields in their average daily doses may be cause of CLL. The risk increases with increasing exposure level (9). Information on the role of chemical exposures in the development of CLL is limited and contradictory because of the lack of data. There is evidence of a slight but significant increase in the risk of all leukemia and chronic lymphocytic leukemia in farmers compared with non-farmers (10, 11). Risk of CLL was significantly increased among those exposed to pesticides and particularly to organophosphates, also carbamates and phosphate (11-13). Many epidemiologic studies have been conducted of benzene-exposed workforces. While the strongest causal association found in these studies is for benzene and Acute Myelogenous Leukemia (AML) and Multiple Myeloma (MM), a causal association has also been found for CLL based upon several studies (14).

MATERIAL AND METHODS
The influence of risk factors in the work environment and the incidence of CLL were examined. Available literature for a period of five years was analyzed (2010-2014). For the same period was made characteristic of patients with CLL according to demographics and occupation, which were registered in the Department of Hematology at the University Hospital - Stara Zagora.

RESULTS AND DISCUSSION
Epidemiological studies were focused on the chemical and physical factors of the working environment. For a period of 5 years (2010-2014) was made characteristic of patients with malignant hemopathy, which were registered in the Department of Hematology at the University Hospital - Stara Zagora. They were reported 179 patients of which 52 patients with proven CLL. Results show an increase in the total number infected in the last two years. We have increased and the number of patients with CLL compared with that of patients with other hematological malignancies expressed in the past two years (Figure 2). After the patients were divided by sex and age, it was established that men are 28 or 54% and women are 24 or 46% of all fifty- two patients with the diagnosis of CLL. In both sexes there is a larger number of patients over 65 years, which confirms the literature data that the disease is more common in adults over 65 years. It is noted that the number of men is more than women, despite the small difference in their number. This is in agreement again with literature data for a high incidence of the disease in males (Figure 3). Data from our study showed that only 22 (42, 3%) of registered patients with CLL (52) have noted occupation in their medical records. Work with pesticides were noted 40, 9% of patients with CLL, while 18, 2% - of exposure to toxic substances (Figure 4). Our results supports the literature data, that pesticide have essential role and proven reason for the increase of risk of CLL. After distribution of patients in residence, it was found that the highest per cents of patients are from Stara Zagora region – 69, 4% and 19, 2 % from Sliven region (Figure 5).

CONCLUSION
For a period of five years (2010-2014) in the Department of Hematology at the University Hospital - Stara Zagora were registered 52 patients with proven chronic lymphocytic leukemia, which are 29% of all hematological malignancies registered for the same period. 69, 4 % were patients from the Stara Zagora region and 19, 2 % from Sliven region. 54 % of them are men and 46% -women. In both sexes was higher number of patients over 65 year.

Only 43 % of registered patients have a history of their profession - 40, 9 % of them worked with pesticides, and 18, 2% with toxic substances.

The introduction of the electronic health record containing information about the occupation of patients and related conditions of employment is essential for occupational risk assessment and diseases.
Figure 1. Peripheral blood smear from a patient with CLL shows lymphocytes as "smudge" cells. The lymphocytes in CLL are fragile and can be damaged when making a smear from a patient with smear preparation producing this smudged or smeared appearance.

Figure 2. Number of patients with CLL and other hematological malignancies

Figure 3. Number of patients divided by sex and age
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