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RESEARCH ARTICLE

Role of various risk factors in occurrence of Acute Myeloid Leukemia

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Abstract

Background: Environmental risk factors play important role in inducing the leukemia either directly or indirectly. Some risk factors are very casual and we usually ignore them but risk factors sometimes plays very crucial role in triggering the leukemia.
Objective: To find out the role of various risk factors in occurrence of AML.
Patients & Methods: Two hundred twenty patients of acute myeloid leukemia (AML) from Deptt. of Pathlogy, Pt. B.D. Sharma University of Health Sciences, Rohtak were carefully studied to know the role of various risk factors in occurrence of AML during 2008-12. The main risk factors considered in present study were prenatal and postnatal risk factors along with occupation of patients and their parents. The various risk factors were analyzed in both group i.e., children (<15 years) and adults (>15 years).
Results: There were 70% cases with prenatal complications having drug intake, exposure to pesticides, exposure to ionizing radiation (IR), electric and magnetic fields (EMF), extremely low-frequency (ELF), and radio frequency (RF), diagnostic X-rays and fetal loss. While 75% patients with postnatal risk factors having smoking, alcohol consumption, pesticides exposure, ionizing radiation, electromagnetic field and infection. Industry (46%) in both groups was the major occupation followed by agriculture (23%) worker in unorganized sector (19%) and self business (12%).
Conclusion: Further study of AML, including occurrence of the leukemia and associated risk factors, is needed in order to confirm these findings and to increase our understanding of this disease.

Introduction:

Cancers are assumed to be multi-factorial diseases which occur when the genetic and environmental factors interact in a multistage sequence. Leukemia as the most common childhood cancer is particularly subjected to this rule. Acute myeloid leukemia (AML) is a heterogeneous disease with distinct histological subtypes likely to have distinct risk factors. AML is the second most common leukemia in children (Bhutani et al., 2002, Kumar et al., 2012). The highest rates of childhood AML occur in Asia and the lowest rates are reported from India and South America (Arora et al., 2009, Cancer Facts, 2013). Numerous genetic risk factors for childhood AML have been defined, including Down syndrome, neurofibromatosis and Fanconi anemia.

Electric and magnetic fields (EMF) are ubiquitous in the modern society. Earth is surrounded by a static magnetic field that varies between 25 μT and 65 μT. Among all the outcomes evaluated in epidemiologic studies of risk factors, there is most evidence of an association for childhood leukemia in relation to postnatal exposures above 0.3–0.4 μT (Bartley et al., 2010). This association is unlikely to be caused by chance but may be partly due to bias, though it is difficult to interpret in the absence of a known mechanism or reproducible experimental support. Most

environmental risk factors have been found to be weakly and inconsistently associated with either form of acute leukemia. But increased risk associated with increased duration and frequency of appliance used was found to be associated with leukemia. The magnitude of the risk depends on the dose of radiation, the duration of exposure, and the age of the individual at the time of exposure. There was no consistent exposure-response relationship in the association with specific subtypes of leukemia. The largest analytic study of childhood AML was found that occupational exposures of either parent to pesticides, paternal exposure to petroleum products and postnatal exposures to pesticides were increased AML in children (Belson et al., 2007). In addition, maternal use of marijuana during pregnancy was associated with an increased risk of AML. Studies of AML in adults have implicated ionizing radiation, solvents, and petroleum products as potential etiologic agents.

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Material & Methods:

This study was performed on 220 patients diagnosed with acute myeloid leukemia from the Department of Pathology, Pt. B.D. Sharma University of Health Sciences, Rohtak during 2008-12. This study was approved by Institutional ethical committee. These patients were evaluated for age of diagnosis, sex ratio, family history, prenatal and postnatal risk factors along with occupation of patients and their parents. A specialized quesnair was developed to record the patient's information.

Results:

Out of 220 patients, 32 were children and 188 were adults (Fig 1). In case of children, there were 21 male and 11 female patients with sex ratio (SR) of 1.9 and in adults, 122 male and 66 female patients with an SR of 1.8. In present study, majority of the cases belonged to six districts i.e. Rohtak, Jind, Bhiwani, Sonipat, Jhajjar, Hissar. Incidence of leukemia were highest in Rohtak district flowed by Jind and Bhiwani (Fig 2). This was due to the vicinity of regional cancer center to these districts. The incidence of AML were greater in urban as compared to rural areas.

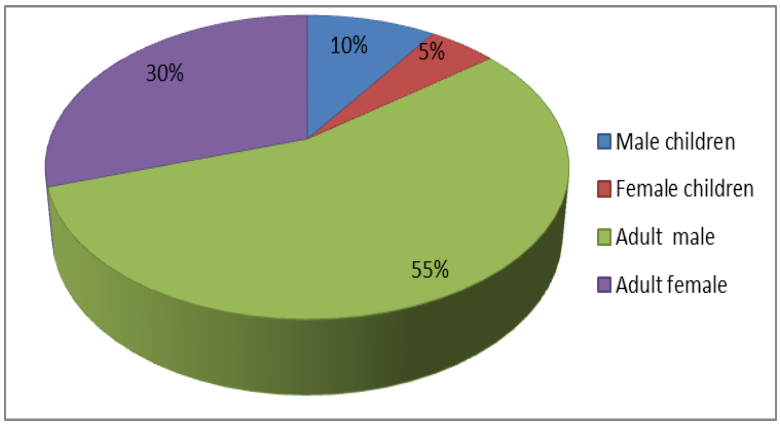

Figure-1. Percentage frequency of patients of Acute Myeloid Leukemia.

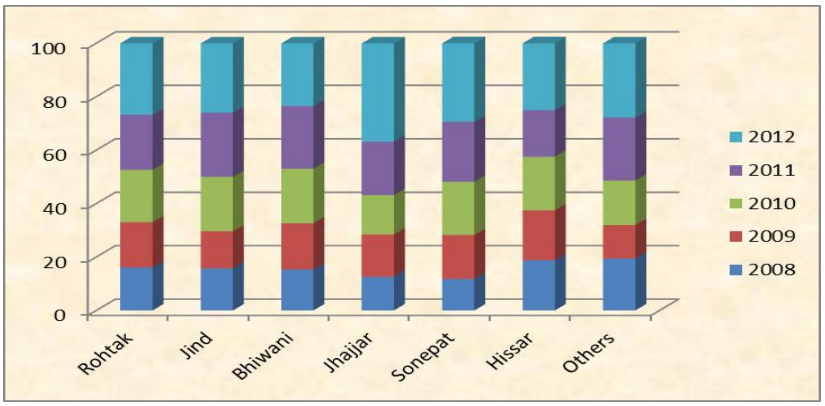

Figure-2. Year-wise percentage frequency of Leukemia during 2008-12.

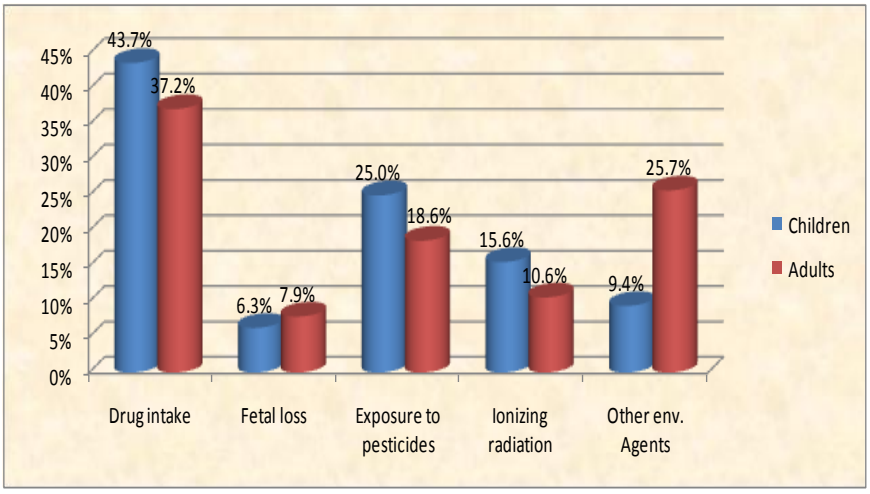

Figure-3. Percentage frequency of prenatal risk factors in mothers of AML.

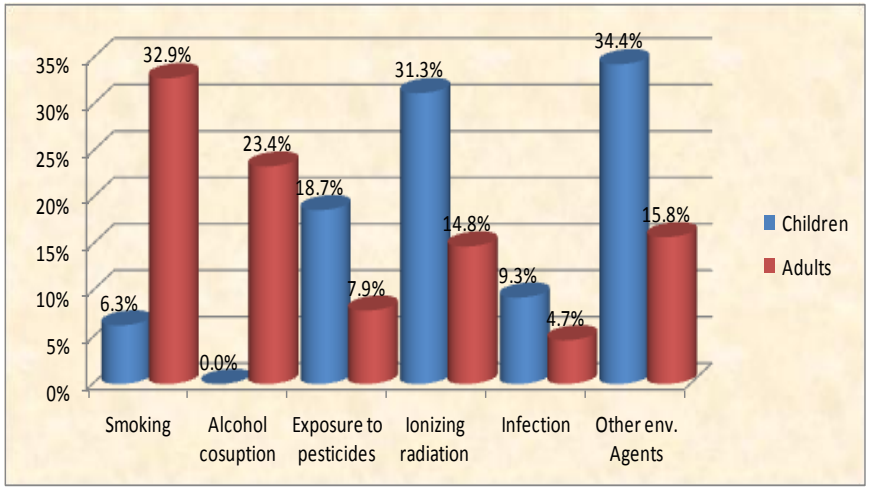

Figure-4. Percentage frequency of postnatal risk factors in AML.

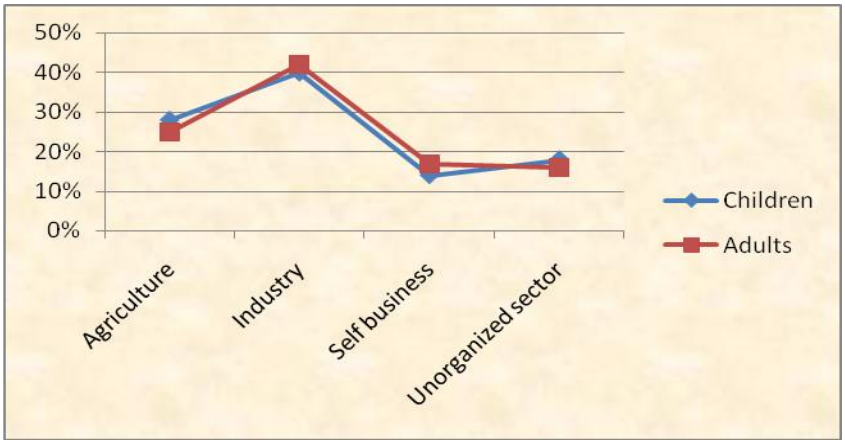

Figure-5. Percentage frequency of occupation as a risk factor in AML.

Prenatal risk factors:

Prenatal history of patients was studied in detail and certain prenatal risk factors considered in the present study were drug intake, exposure to pesticides, exposure to ionizing radiation (IR), electric and magnetic fields (EMF), extremely low-frequency (ELF), and radio frequency (RF), diagnostic X-rays and fetal loss. Seventy percentage patients were found with prenatal risk factors. Drug intake was noted in mothers of 42.2% patients. Fetal loss was found in 9.7% patients followed by exposure to pesticides in 14.3%. Diagnostic X-rays was found in 7.1% mothers during pregnancy and exposure to ionizing radiation like exposures related to mobile telephone and other devices was found in only 4.5%. Other environmental risk factors were 22.2%.

Prenatal risk factors in children:

Alcohol, cigarette, and illicit drug use has an increased risk for AML, particularly among very young children, associated with maternal alcohol consumption during pregnancy. Maternal marijuana use before and during pregnancy has been associated with childhood AML. Most children's exposure to pesticides was from home, lawn and garden use. Other sources of exposure were included local agricultural applications, contaminated food, parental occupation and pet products. Mothers of 43.7% children had history of drug intake. Pesticides exposure during agriculture activities was found in parents of 25% children. Repeated exposure to diagnostic X-rays and ultrasound was noted in mothers of 15.6% children. Mothers of 6.3% children had history of fetal loss more than two times. No risk factor was noted in parents of 9.4% children (Fig 3).

Prenatal risk factors in adults:

The chemical classes most commonly associated with childhood leukemia are hydrocarbons and pesticides. Hydrocarbons are organic compounds made up primarily of carbon and hydrogen atoms. Examples of hydrocarbon compounds include gasoline and trichloroethylene (spot remover). Hydrocarbons are found in many household and industrial products including paint removers and thinners and solvents, which are used to dissolve other chemical substances. The most widely recognized hydrocarbon is benzene, a ubiquitous chemical used in the manufacture of paints and plastics and as a constituent in motor fuels and hobby glues. It is also formed during incomplete combustion of fossil fuels (i.e., petroleum products, coal). Benzene is a known human carcinogen. It has a strong positive exposure-response relationship with leukemia, particularly AML.

Mothers of 37.2% adults had history of drug intake. Pesticides exposure during agriculture activities was found in parents of 18.6% adults. Repeated exposure to diagnostic X-rays and ultrasound was noted in mothers of 10.6% adult patients. Mothers of 7.9% adult patients had history of fetal loss more than two times. No risk factor was noted in parents of 25.7% adult patients (Fig 3).

Postnatal risk factors:

Various postnatal risk factors considered in the present study were smoking, alcohol consumption, pesticides exposure, ionizing radiation, electromagnetic field and infection. There were 75% of acute myeloid leukemia cases who had shown postnatal complications. Frequency of various risk factors in AML were calculated as smoking in 20%, alcohol consumption in 16.8%, pesticides exposure in 15%, exposure to ionizing radiation in 12.1%, exposure to electromagnetic field in 6.1%, infection in 9% and 21% including other environmental agents.

Postnatal risk factors in children:

The most prominent postnatal risk factors in children were exposure to ionizing radiation, pesticides exposure and infection. Twenty five percent children had history of repeated x-rays exposure. Six point three percent children were found playing near power houses and high voltage electrical lines. Pesticides exposure during household activities was found in 18.7% children. The history of infection (pneumonia) was noted in 9.3% children. Smoking was noted in 6.3% children. The risk factors were not known in 34.4% cases (Fig 4).

Postnatal risk factors in adults:

Smoking and alcohol were most prominent factors in adult patients. Thirty two point nine percent adult patients had habits of smoking. The alcohol addiction was found in 23.4% adult patients. Pesticides exposure during agriculture activities was noted in 7.9% adults. Nine point five percent adult patients had exposure to x-rays many times. Five point three patients had residence near high voltage electrical lines and 4.7% patients had history of infection and 15.8% had other risk factors (Fig 4).

Occupation of patients:

Occupational exposures examples include RF, PVC welding machines, plasma etchers, and military and civil radar systems, all operating at different frequencies. Occupation and place of work of patients and their parents was carefully analyzed to know their role in the occurrence of AML. In the present investigation, main categories of occupation were agriculture, industry, workers in unorganized sector, and self business. Industry (46%) was the major occupation followed by agriculture (23%), worker in unorganized sector (19%) and self business (12%).

Occupation of children:

Forty percent children and their parents were living near/working in industries like manufacturing paint and fertilizer. Twenty eight percent children and their parents were engaged in different agriculture activities. The self business likes candle making, carpeting, and printing was noted in 14% patients and their parents. Eighteen percent children and their parents were working in unorganized sector like transport, restaurant and press (Fig 5).

Occupation of adults:

Forty two percent patients were living near/working in industries like manufacturing paint, pesticides and dye. Twenty five percent patients were engaged in agriculture. The self business likes carpeting, and printing was noted in 17% patients. Sixteen percent patients were working in unorganized sector like transport, restaurant and brick making (Fig 5)

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Discussion:

Leukemia is not a single disease but a group of diseases perhaps with many different causes. Although the cause in most cases of childhood leukemia is not known, certain factors have been suggested to contribute to susceptibility. The causative factors may be like smoking, high birth weight, diet, high socioeconomic status, electromagnetic field, being exposed to radiation, past treatment with chemotherapy or other drugs that weaken the immune system, having certain changes in genes or genetic disorders, such as Down syndrome and maternal alcohol consumption (Sandler et al., 1997, Benson et al., 2007, Hassanzadeh et al., 2011).

The risk factors considered in present study were categorized as prenatal and postnatal risk factors. Occupation of patients and their parents was also studied to know the role of environment in occurrence of disease. Prenatal risk factors during pregnancy considered in present study were drug intake, exposure to pesticides, exposure to ionizing radiations and fetal loss. Mothers of 43.7% children and 37.2% adult patients had history of drug intake before or during pregnancy. Exposure to pesticides was noted in mothers of 25% children and 18.6% adults. History of fetal loss was noted in mother of 6.3% children and 7.9% adult patients. Conflicting results have been reported from studies of the relationship between maternal history of fetal loss and risk for ALL or AML (Robinson, 1994, Yeazel et al., 1995, Ross et al., 1997). Prenatal exposure to ionizing radiation was noted in 15.6% children and 10.6% adult patients of AML. Several studies have assessed the risk in utero exposure to diagnostic x-rays and an increased risk of AML (Miller, 1995, Schmitz et al., 1997, Doll et al., 1997).

Various postnatal risk factors considered in the present study were smoking, alcohol consumption, pesticides, ionizing radiation, electromagnetic field and infection. Smoking was observed in 6.3% children and 32.9% adults. A study has shown 2-3 times higher risk of leukemia in smokers than non-smokers (Pogoda et al., 2002). The alcohol addiction (23.4%) was found as another major risk factor in adult patients. However; some studies have found increase risk of AML in children whose parents had habits of alcohol (Van Duijn et al., 1994, Shu et al., 1996). A statistically significant increased risk (OR=1.5) for acute myeloid leukemia was associated with active smoking (Kasim, 2005). Reports on association of alcohol drinking and leukemia have not been consistent and there has been conflicting findings (Balasubramaniam et al., 2013). A population-based case-control study in 11 Italian areas found a non-significantly inverse association for moderate levels of total alcohol and wine intake, but increased risks at high levels (Gorini, 2007). Thirty one point three percent children and 14.8% adults had much exposure to x-rays in present study. Postnatal exposure to ionizing radiation has been shown to increase the risk of leukemia in several studies (Miller, 1995, Schmitz et al., 1997).

Occupation of parents has been shown to increase the risk of leukemia (Buckley et al., 1989). In the present investigation, main categories of occupation were agriculture, industry, workers in unorganized sector, and self business. Industrial work was a major occupation in children (40%) as well as adults (42%). The incidence of hematological malignancies were greater in urban as compared to rural areas. The possible explanation is that the rural and urban populations are different with regard to environmental and socioeconomic factors. Urban cities in Haryana are industrialized and fairly populated. Socioeconomic status of people is higher and dietary habits and lifestyle tends to tilt toward Western styles. In rural areas, on the other hand, people stick to traditional eating habits

and lifestyle. These factors may be responsible for the relative differences in the incidence of hematological malignancies in urban versus rural population.

The second major occupation in children and adults was agriculture. Increased risk of AML in children has been shown by occupation exposure to pesticides during agriculture activities (Infante-Rivard et al., 1999, Menegaux et al., 2006). The patients and their parents were engaged in industries like manufacturing paint, fertilize, dye and pesticides. Specific occupations which have been reported in earlier studies include metal manufacturing, textiles and pharmacist (Van Steensel-Moll et al., 1985, Savitz et al., 1990). Fourteen percent children and 17.8% adults had their own business. Patients and their parents were engaged in profession like carpeting, printing and candle making. Schuz et al have reported increased risk of AML in mother exposed to paint or lacquer during the perception period (Schuz et al., 2000). The remaining patients and their parents were found working in unorganized sector like transport, press and brick making.

Conclusion:

Identifying risk factors for leukemia (e.g., prenatal, postnatal, occupation and environmental) is an important step in the reduction of the overall burden of the disease. In present study, prenatal and postnatal risk factors were found strongly associated with the development of AML. In prenatal risk factors, drug intake and exposure to pesticides was major risk factor in children as well as in adults while in postnatal risk factors exposure to ionization radiation in children and smoking in adults were major risk factors. So, the study will play important role in assignment of possible risk factors and in attempt to determine the role of risk factors in occurrence of acute myeloid leukemia in Haryana.

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