Increased Risk of Childhood Acute Lymphoblastic Leukemia (ALL) by Prenatal and Postnatal Exposure to High Voltage Power Lines: A Case Control Study in Isfahan, Iran

Maral Mazloomi Tabrizi, Sepideh Arbabi Bidgoli*

Abstract

Childhood acute lymphoblastic leukemia (ALL) is one of the most common hematologic malignancies, accounting for one fourth of all childhood cancer cases. Exposure to environmental factors around the time of conception or pregnancy can increase the risk of ALL in the offspring. This study aimed to evaluated the role of prenatal and postnatal exposure to high voltage power lines on the incidence of childhood ALL. This cross-sectional case control study was carried out on 22 cases and 100 controls who were born and lived in low socioeconomic families in Isfahan and hospitalized for therapeutic purposes in different hospitals from 2013-2014. With regard to the underlying risk factors, familial history and parental factors were noted but in this age, socioeconomic and zonal matched case control study, prenatal and childhood exposure to high voltage power lines was considered as the most important environmental risk factors of ALL (p=0.006, OR=3.651, CI 95%, 1.692-7.878). As the population was of low socioeconomic background, use of mobiles, computers and microwave was negligible. Moreover prenatal and postnatal exposure to indoor electrically charged objects was not determined to be a significant environmental factor. Thus, pre and post natal exposure to high voltage power lines and living in pollutant regions as well as familial influence could be described as risk factors of ALL for the first time in a low socioeconomic status Iranian population.

Keywords: Leukemia - acute lymphoblastic leukemia - childhood cancer - electromagnetic field - Isfahan - Iran
Materials and Methods

Population study
A case-control cross sectional study was carried out among 22 newly diagnosed ALL and 100 normal children who were all <12 years, born and grown up in Isfahan. Leukemia were identified from both self-reports registration and ALL was confirmed by evaluating their pathological reports. Exclusion criteria for cases and controls were lack of access to the parents, birth and living out of Isfahan and having moderate and higher socioeconomic state. The control group was matched with cases for age ±5 years who born and lived in the same region.

Electromagnetic fields (EMF): Living near high voltage power lines, using mobiles, computers, microwave and all indoor electrically charged objects were considered for inclusion as a potentially important environmental factor in the present study (Sohrabi, 2010).

Identification of environmental resources
Exact living and working addresses of cases and controls were recorded and matched with the map of factories generating PAHs, dioxins, pesticides and other pollutants. A complete list of factories that release toxicants with hormone-like effects was provided before starting the study.

The families who lived within 4 km from the pollutant factories were considered for assessment as high risk families. Occupational exposures to chemicals, radiation, using plastic water and food containers through validated questionnaire.

Identification of background variables
Demographical variables were obtained from specific questionnaire items: Delivery related factors including place of birth, paternal and maternal ages at delivery, BMI, education, job, socioeconomic states, physical activity, Personal history of any disorders, birth weight at delivery; familial history of leukemia, mother’s irregular menstruation, marriage related factors including marital status of parents, age at marriage.

Maternal related factors
Information on hormone use was obtained from specific questionnaire items. They covered questions on ever and current use of oral contraceptive pills (OCPs), the brand names, age at start and total duration of the use. Other methods of contraception were recorded including use of intrauterine device, tubectomy and use of progestins. Pregnancy related factors including number of full-term pregnancies, age and maximum weight gain at each pregnancy, months of breast feeding at each delivery, history of abortion induction were recorded. History of infertility covered questions on years of infertility, i.e., more than 2 years without birth controlling methods, use of ovulation stimulating drugs, hormone therapy or history of in vitro fertilization. Patients were asked their gynecological disorders including ovarian cysts, uterine fibroadenoma, irregular menstruation, hyrsutism and other disorders.

Statistical methods
Values were expressed as percent per population or as the mean standard deviation. To assess associations between parametric variables Student t-test and to evaluate nonparametric data, the chi square test was used. Relative risks and odds ratios were calculated by the Cochran-Mantel-Haenszel statistics using SPSS 16 and the odds ratios were reported for this case control retrospective study. When the odds ratio in cases was >1, if the probability values was <0.05 and when the 5% confidence interval of the true odds ratio was greater than 1, then we interpreted it as significant risk factor. When the odds ratio in controls was <1, if the probability values was <0.05 and when the 5% confidence interval of the true odds ratio was less than 1, then we interpreted it as protective factor.

Results
Electromagnetic fields (EMF): In this age, socioeconomic and zonal matched case control study prenatal and childhood exposure to high voltage power lines was considered as the most important environmental

| Characteristics                                      | Case (n=22) | Control (n=100) | P-Value | OR   | CI 95% Lower | Upper |
|------------------------------------------------------|-------------|-----------------|---------|------|-------------|-------|
| Prenatal exposure to high voltage power lines         |             |                 |         |      |             |       |
| Yes                                                  | 4 (18.18%)  | 3 (3%)          | 0.006   | 3.651| 1.692       | 7.878 |
| No                                                   | 18 (81.81%) | 97 (97%)        |         |      |             |       |
| Neonatal and childhood exposure to high voltage power lines (>4yrs) |             |                 |         |      |             |       |
| Yes                                                  | 4 (18.18%)  | 3 (3%)          | 0.006   | 3.651| 1.692       | 7.878 |
| No                                                   | 18 (81.81%) | 97 (97%)        |         |      |             |       |
| Keep food and water in plastic containers            |             |                 |         |      |             |       |
| Yes                                                  | 13 (59.09%) | 22 (22%)        | 0.001>  | 3.590| 1.689       | 7.631 |
| No                                                   | 9 (40.90%)  | 78 (78%)        |         |      |             |       |
| Living near polluting factories (<4 km)              |             |                 |         |      |             |       |
| Yes                                                  | 5 (22.72%)  | 5 (5%)          | 0.006   | 3.265| 1.529       | 6.971 |
| No                                                   | 17 (77.27%) | 95 (95%)        |         |      |             |       |
| Sunlight exposure (<2hrs)                            |             |                 |         |      |             |       |
| Yes                                                  | 16 (72.72%) | 47 (47%)        | 0.029   | 2.497| 1.048       | 5.952 |
| No                                                   | 6 (27.27%)  | 53 (53%)        |         |      |             |       |
High Voltage Power Line and Polluting Factory Influence on ALL in Isfahan, Iran

risk factors of ALL (p=0.006, OR=3.651, 95%CI 1.692-7.878). In fact 18.8% of ALL children had continuous exposure to high voltage power lines from prenatal time to 4th age. As the population study was from low socioeconomic state, using mobiles, computers, microwave was negligible. Moreover prenatal and postnatal exposure to all indoor electrically charged objects were not detected as significant environmental factors in present study.

Identification of environmental resources: Consumption of food and water from plastic containers in these children was considered as the second important risk factor (p<0.001, OR=3.651, 95%CI 1.692-7.878). In fact 18.8% of ALL children had continuous exposure to high voltage power lines from prenatal time to 4th age. As the population study was from low socioeconomic state, using mobiles, computers, microwave was negligible. Moreover prenatal and postnatal exposure to all indoor electrically charged objects were not detected as significant environmental factors in present study.

Identification of familial background factors: Out of 50 evaluated background factors, familial history of leukemia was considered as the the most important risk factor of ALL in this young (<12 years) population (p<0.001, OR=8.143, 95%CI 4.986-13.3). Parental history of occupational exposures was also considered as the second important risk factor of ALL (p<0.001, OR=3.651, 95%CI 1.692-7.878). For some childhood cancers, such as acute lymphoblastic leukemia (ALL), there is evidence of an embryonic cell of origin (Marshall et al., 2014) therefore we assessed the prenatal

Table 2. Comparison of Parental/Familial risk factors between ALL Cases and Controls

| Characteristics                  | Case (n=22) | Control (n=100) | P-Value | OR  | CI 95% Lower | CI 95% Upper |
|----------------------------------|------------|----------------|---------|-----|-------------|-------------|
| Familial history of leukemia     |            |                |         |     |             |             |
| Yes                              | 8 (36.36%) | 0 (0%)         | <0.001  | 8.143* | 4.986       | 13.30       |
| No                               | 14 (63.63%)| 100 (100%)     |         |     |             |             |
| Parental history of occupational exposure |         |                |         |     |             |             |
| Yes                              | 10 (45.45%)| 2 (2%)         | <0.001  | 7.639* | 4.230       | 13.79       |
| No                               | 12 (54.54%)| 99 (99%)       |         |     |             |             |
| Exposure to X-rays around the time of conception or pregnancy |         |                |         |     |             |             |
| Yes                              | 3 (13.63%) | 40 (40%)       | 0.019   | 4.222* | 1.172       | 15.21       |
| No                               | 19 (86.36%)| 60 (60%)       |         |     |             |             |
| Maternal severe stress around the time of conception or pregnancy |         |                |         |     |             |             |
| Yes                              | 6 (27.27%) | 6 (6%)         | 0.002   | 3.438* | 1.665       | 7.096       |
| No                               | 16 (72.72%)| 94 (94%)       |         |     |             |             |
| Parental consanguinity           |            |                |         |     |             |             |
| Yes                              | 8 (36.3%)  | 14 (14%)       | 0.014   | 2.597* | 1.244       | 5.42        |
| No                               | 14 (63.63%)| 86 (86%)       |         |     |             |             |
| Menstrual irregularities in mothers before conception |         |                |         |     |             |             |
| Yes                              | 11 (50%)   | 26 (26%)       | 0.027   | 2.297* | 1.095       | 4.821       |
| No                               | 11 (50%)   | 74 (74%)       |         |     |             |             |

Figure 1. Ranking of ALL Risk factors According to the Odds Ratios

Discussion

Recent evidences according to epidemiological studies, support a clear association between socioeconomic status and increased risk of childhood cancers (Hashemizadeh et al., 2013), (Njoku et al., 2013) especially in ALL (Metayer et al., 2014). This study tried to find the possible risk factors of ALL in low socioeconomic population in industrial regions of Isfahan by focusing on the role of electromagnetic fields for the first time in this group of patients in Iran.

Several local epidemiological studies have been conducted in different provinces of Iran including Mazandaran (Tahmasby et al., 2013), Golestan (Rajabli et al., 2013) and Khorasan Razavi (Hashemizadeh et al., 2013)on the prevalence of Leukemia and its possible risk factors.Although the obtained findings in the last study showed clear differences in the incidence rates of Leukemia based on age, gender, residence, and type of malignancy, ALL was considered as the most prevalent type of leukemia. For this reasons we focused on the paternal, maternal background factors, prenatal and postnatal environmental exposures in Isfahan as a city with higher levels of air pollution (Rashidi et al., 2013) (Janghorbani et al., 2013) and soil pollution (Mohajer et al., 2013).We considered here 11 most significant causes and considered the specific role of prenatal X-ray exposure before of at conception time, maternal severe stress in pregnancy, parental consanguinity and menstrual irregularities in the mothers of ALL children when compared with normal children.
factors in this study at the first part of assessments and found the dramatic carcinogenic effects of living near high voltage power lines in prenatal and postnatal periods.

We observed in present setting that the incidence of leukemia in first degree family of patients may increase the ALL risk more than 8 times (p<0.001, OR=8.143, 95%CI 4.986-13.3) and considered the other factors (Figure 1). This results confirm the role of family cancer history which was previously considered in a population-based case-control study in chronic lymphocytic leukemia cases. This study in Baltimore suggested a genetic component for leukemia occurrence in several case families, although the majority of cases of leukemia appeared to be sporadic (Zierhut et al., 2012).

In present work we considered the etiology of ALL for the first time in Iranian population but despite the significant role of family history, the rest of children 14(63.63%) didn’t have any history of malignancy in their first degrees and urge the scientists to evaluate the role of environmental factors.

The second ranked important background factor was parental occupational exposures. Out of 22 patients, 10 children (45.45% vs 2%) showed paternal exposure to chemicals (diesel oil, gasoline, paints, insecticides, pesticides, herbicides, and chemical fertilizers) before and at the conception time or paternal working experiences in agriculture and forestry before pregnancy, leather processing, decoration, and vehicle repair (p<0.001, OR =7.639, 95%CI 4.23-13.794) in accordance with results of parallel work in China (Shi et al., 2013).

In conclusion, his work has defined the forces of environmental exposures especially continuous pre and postnatal exposure to high voltage power lines and living in pollutant regions through the parents or children as well as the role of previously described risk factors of ALL for the first time in low socioeconomic Iranian population. We confirmed here a new risk factor for ALL and suggest the hypothesis on embryonic origin of many other cancers which should be assessed in next studies in larger case control studies.

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