Risk factors of childhood leukemia at Tripoli medical center in Libya

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Abstract
This study was conducted to investigate the risk factors of leukemia childhood at Tripoli medical center department of Pediatric Oncology. Forty one patients participate in this study their ages between 2-13 years (26 Males and 15 Females). Based on questionnaire to the patients family about the risk factors 17% of the families have no idea about the type of the leukemia 68% of the participated patients suffering from acute lymphocytic leukemia (ALL) and 15% from acute myeloid leukemia (AML). Our results show that the paternal age may increase the risk factor of child leukemia as 37% of the parent ages more than 40 years old. Arranging of the child in their family can also affect the development of the leukemia as about 29% of leukemic child was first or only one child in their family. Also our data shows that 25% of the risk factors due to smoking, housing location near benzene station, industrial regions, weapon stores and the high electric pressure. Other factors like fast food represent about 22% and the household solvent represent 9% and soda drink represent 8%. The risk factors play an important role in increasing the incidence of leukemia however the contribution of these factor participating as complementary to each other instead of each factor alone. Doctors, nurses and pharmacists should working together around the world to continue to improve outcome for children diagnosed with pediatric cancer.

1. Introduction

Leukemia refers to cancer of white blood cells (also called leukocytes or WBCs) When child has large number of abnormal white blood cells are produced in bone marrow. These abnormal WBCs crowed the bone marrow and flood the blood stream, but they cannot perform their proper role of protecting the body against disease because they are defective. Leukemia is often described as being either acute (fast growing) or chronic (slow growing) as published by [1,2,3].

1. Acute lymphocytic (lymphoblastic) leukemia (ALL):
2. Acute myelogenous leukemia (AML)
3. Hybrid or mixed lineage leukemia
4. Chronic myelogenous leukemia (CML)
5. Chronic lymphocytic leukemia (CLL3) Juvenile myelomonocytic leukemia (JMML)

As leukemia progresses, the cancer interferes with the body's production of other type of blood cells, including red blood cells and platelets.

This results in anemia and bleeding problems, in addition to increased risk of infection caused by white cells abnormalities. In most cases, the leukemia invades the blood fairly quickly. From there it can go to other parts of the body such as the lymph nodes, spleen, liver, central nervous system (the brain and spinal cord), testicles, or other organs as shown by Howlader et al. [4]

There were 470 new cases of childhood leukemia recorded in the UK in 2003. Recorded incidence of childhood leukemia has risen in Europe since the 1970s due in most part to a small increase in ALL in the under 5s as discussed by Steliarova et al. [5]. Leukemia may affect children of any age, but each type commonly affects a particular age group as shown by Forestier [6].

Statistics have shown that leukemia common malignancies in Arabic countries for year 2004, Libya takes the 40th world rank as shown in table 1.

### Table 1. Common Malignancies in Arabic Countries

<table>
<thead>
<tr>
<th>Arab Country</th>
<th>Rate</th>
<th>World Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iraq</td>
<td>12.6</td>
<td>1</td>
</tr>
<tr>
<td>Jordan</td>
<td>8.4</td>
<td>4</td>
</tr>
<tr>
<td>Yemen</td>
<td>6.9</td>
<td>10</td>
</tr>
<tr>
<td>Lebanon</td>
<td>6.8</td>
<td>11</td>
</tr>
<tr>
<td>Omen</td>
<td>6.7</td>
<td>12</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>6.4</td>
<td>15</td>
</tr>
<tr>
<td>Egypt</td>
<td>5.1</td>
<td>28</td>
</tr>
<tr>
<td>Bahrain</td>
<td>4.9</td>
<td>30</td>
</tr>
<tr>
<td>Sudan</td>
<td>4.6</td>
<td>33</td>
</tr>
<tr>
<td>Somalia</td>
<td>4.5</td>
<td>34</td>
</tr>
<tr>
<td>Kuwait</td>
<td>4.1</td>
<td>38</td>
</tr>
<tr>
<td>Libya</td>
<td>3.9</td>
<td>40</td>
</tr>
<tr>
<td>Qatar</td>
<td>3.7</td>
<td>42</td>
</tr>
<tr>
<td>Syria</td>
<td>3.7</td>
<td>42</td>
</tr>
</tbody>
</table>

### Table 2. Characteristics of the studied population

<table>
<thead>
<tr>
<th>Patients include</th>
<th>41</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>26 (63%)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (37%)</td>
</tr>
<tr>
<td>Type of Leukemia</td>
<td></td>
</tr>
<tr>
<td>ALL</td>
<td>28 (68%)</td>
</tr>
<tr>
<td>AML</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Unknown Type</td>
<td>7 (17%)</td>
</tr>
<tr>
<td>Age</td>
<td>2-13 year</td>
</tr>
</tbody>
</table>

Incidence of varies leukemia type for both gender was consistently higher among males (approximately 20%) relative to females. The sample poled in our study divided in to two groups (ALL, AML) according to the types of leukemia Where the ALL represent about 68% which is the most predominant type of leukemia in children who are younger than 15 years of age and AML is 15% of the cases, which confirm with many studies [7,8,9] the remaining percentage (17%) was represent unknown leukemia type which indicates that leukemic child families has low level of education status.

Figure1 shows the effect of paternal age which is more than 40 years and maternal age which is more than 35 years on the increasing the risk of childhood leukemia where the percentage of leukemic child who have father age more than 40 years was about 37% while percentage of leukemic child who have mother age more than 35 years was about 29% which confirm that the parents age of children at their birth have effect on increasing the risk of leukemia in those children as many previous studies [10,11] that suggest paternal age (<40 years) have significant effect on increasing risk of leukemia in their children and maternal age (<35 years) have slight effect on increasing risk of leukemia, some study show no significant association between paternal and maternal age and risk of leukemia while other study that agreed with our results [12].

### Figure 1. Percentage of leukemic child according to parents age.

- Maternal age more than 35 years: 71%
- Mother age less than 35 years: 29%
- Father age more than 40 years: 63%
- Father age less than 40 years: 37%

The arranging of child in their family have effect on development of leukemia as shown in Figure 2 about 29% of leukemic child was first or only one child in their family as published by Robson and Sandler [10,11] which is
agreed with previous study that show an increasingly later position in the birth order was associated with a statistically significantly decreased risk of leukemia.

![Figure 2. Percentage of leukemic child according to their arranging in their family](image)

As shown in the Figure 3 the percentage of leukemic child according to their weight at birth About 27 % of leukemic child was born at weight more than 4 kg and other represent 73%, 27% is a percentage to be considered as a Compelling evidence suggests that childhood leukemia often originates in uterus.

![Figure 3. Percentage of leukemic child according to their birth weight](image)

According to previous study show the Birth weight is one of the pregnancy-related risk factors that have been associated with leukemia risk, but the association has remained poorly characterized

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A birth weight of (4kg) or more was associated with a statistically significantly higher risk of ALL than a birth weight of less than (4kg). Using a large dataset from nationwide population-based registers. In Denmark, Sweden, Norway, and Iceland, they observed a statistically significant 26% increase in risk of ALL per 1-kg increase in birth weight. Although this observation is consistent with previous findings [13, 14].

![Figure 4. Percentage of risk factors among the population](image)

### 3.1. Smoking

Smoking is considered to be one of the major risk factor direct smoking and passive smoking as a result of chemical contained in cigarette considered to be toxic or carcinogenic, like benzene formaldehyde, aromatic amines, polycyclic aromatic hydrocarbons (PAHs) and nitrosamines and radioactive compounds like Polonium-210 [15]. Benzene has been shown to affect the blood-forming system at low levels [16] and formaldehyde has been shown to increase leukemia risk among exposed adults[17]. Smoking is causatively linked with adult leukemia [18] and passive smoking (SHS) is qualitatively similar in its chemical constituents to mainstream smoke indicating that SHS exposure has the potential to cause adverse effect on the hematopoietic System.

Children aged 6 to 11 years were reported to have urinary concentrations of specific carcinogen nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) nearly four times those of adult nonsmokers as published by Bernert et al. [19] indicating that children are less able to avoid exposure to SHS than Adults. Smoking has also been shown to affect sperm morphology, motility, and concentration and to increase oxidative damage to sperm DNA. Together, these findings indicate that parental smoking is a potential risk factor for childhood leukemia that could induce DNA damage and mutation pre- and postnatal. Through 2009, 20 studies [19,20] investigated maternal smoking and Childhood. ALL, with three studies reporting statistically positive associations, two study [21] reporting statistically negative associations and the remainder reporting non-significant association. Among the 18 studies on paternal smoking, eight showed increased risks of childhood ALL for at least one index (exposure level or time period) of paternal smoking which is agreed with our result as meshed before, so that possible reason for this may be that a true association exists.

### 3.2. Pesticide

Several studies have linked leukemia to pesticides. Two
recent reviews concluded that pesticide exposure may be a cause of leukemia. Parental exposure to pesticides may contribute to childhood cancer risk. Through the Agricultural Health Study, a prospective study of pesticide applicators in Iowa and North Carolina, examined childhood cancer risk and associations with parental pesticide application. Identifying information for 17,357 children of Iowa pesticide applicators was provided by parents via questionnaires (1993–1997) and matched against the Iowa Cancer Registry. This study shows an increased risk of cancer was detected among children whose fathers did not use chemically resistant gloves [odds ratio (OR) = 1.98; 95% CI, 1.05–3.76] compared with children whose fathers used gloves. Of 16 specific pesticides used by fathers prenatally, ORs were increased for alien (OR = 2.66), dichlorvos (OR = 2.06), and ethyl dipropylthiocarbamate (OR = 1.91). Identification of excess lymphoma risk suggests that farm exposures including pesticides may play a role in the etiology of childhood lymphoma as discussed by Daniels et al [22].

3.3. High-Voltage Power

The Living near high-voltage power lines raises children's risk of leukemia by 69%, a British study shows. That doesn't prove that power lines cause the deadly blood cancer, the study's authors are quick to point. Despite 30 years of research, scientists still can't come up without plausible reason why the weak magnetic fields near power lines might cause leukemia. Gerald Draper, DPhil, director of the childhood cancer research group at Oxford University, led the study. Draper's team compared more than 29,000 children with cancer, including 9,700 children with leukemia, to age-, sex-, and birthplace-matched children without cancer. The children's birth homes were located on the power grids England and Wales. Compared with children who lived more than 600 meters from a high-voltage power line, those who lived within 200 meters of the power lines had a 69% greater risk of leukemia. Those living 200 to 600 meters from power lines had a 23% higher risk of leukemia. The findings appear in the June 4 issue of the British Medical journal. There is a slight tendency for the birth addresses of children with leukemia to be closer to these lines than those of children matched for comparison, Draper and colleagues write. "We have no satisfactory explanation for our results in terms of causation by magnetic fields, and the findings are not supported by convincing laboratory data or any accepted biological mechanism. There are many theories about how power lines might cause leukemia [23]. The most obvious one is that the magnetic fields created by power lines somehow make cancer cells grow in susceptible people.

3.4. Fast Food

Eating fast food may cause cancer. The state of California is suing nine top fast food manufacturers, including Burger King, Heinz and McDonald's; over their reluctance to issue warnings that some of their snacks could contain the potentially cancer-causing chemical acrylamide. Acrylamide was found to be linked to cancer in 2002.

3.5. Soft Drink

Recent studies, however, have suggested that drinking just one can of diet soda per day can massively increase the chances of getting certain medical conditions. The men have been said to have an increased risk of getting non-Hodgkin lymphoma as well as multiple myeloma, and women have been said to have an increased risk of leukemia. The study of diet drinks has been ongoing for many years, but this is one of the most in-depth studies on the subject, and the results that have been released are incredibly shocking.

The study took into account the results of over 77,000 women, and almost 50,000 men and in total, gave scientists over two million people-years worth of data. As well as being the largest study with regards to people numbers, this one has also shown to be the most in-depth look at how the effects of diet drinks can affect people, and to be more precise, their health over the long term. “One diet soda a day increases leukemia, multiple myeloma and non-Hodgkin lymphomas” In the course of this study it was shown that one can of diet pop, equal to 355ml, per day will give men and women a 42% increased chance of getting leukemia. For the men, this daily dose of fizzy pop also leads to over 100% increased risks of getting multiple myeloma, and a 31% higher chance of getting non-Hodgkin lymphoma [24].

3.6. Weapons Stores

With regard to housing near the stores of weapons had been an explosion during the revolution of February 17, we wish that in the near future all the damages that have occurred during the war are treated in a healthy manner. Based on studies conducted on the Iraq war, we used them as a reference for our project and we opted to choose this because of the similarities between the two wars. Similarly high values are reported from Fallujah, a city that was fiercely contested in the 2003 war. According to the Heidelberg study, the concentration of lead in the milk teeth of sick children from Basra was almost three times as high as comparable values in areas where there was no fighting. Never before has such a high rate of neural tube defects ("open back") been recorded in babies as in Basra, and the rate continues to rise. The number of hydrocephalus ("water on the brain") cases among newborns is six times as high in Basra as it is in the United States, the study concludes [25]. Jawed al-Ali (1999) has worked as a cancer specialist at the Sadr Teaching Hospital (formerly the Saddam Hospital), housed in a sinister-looking building in Basra. He remembers the period after the first Gulf war over Kuwait. "It isn't just that the number of cancer cases suddenly increased. We also had double and triple cancers, that is, patients with tumors on both kidneys and in the stomach. And there were also familial clusters, that is, entire families
that were affected.” He is convinced that this relates to the use of uranium ammunition. “There is a connection between cancer and radiation. Sometimes it takes 10 or 20 years before the consequences manifest themselves.

3.7. Benzene

Genotoxic potential of benzene on bone marrow was first proposed a century ago. According to study in a group of 22,458 children who died from cancer between 1953 and 1980 to examine the relationship between the birth and death addresses of these children and sites of potential environmental hazards Childhood cancers were found to be geographically associated with industrial atmospheric effluents, namely petroleum-derived volatiles, kiln and furnace smoke and gases, and emissions from internal combustion engines as shown by Knox [26]. Our study shown that percentage of child who affected by benzene was 3% as shown in Figure 4.

3.8. Abortion

Abortion represents about 8% as in Figure 4, According to study in USA [10,27] approximately 2-5 fold increase in risk of leukemia in children whose mothers have abortion before. Several studies have reported associations between childhood cancers And surrogate measures of exposure to motor vehicle exhausts including traffic density, vehicle density, and estimated concentrations of nitrogen dioxide and benzene For example, in 1989, a study in Denver, Colorado that assigned traffic density measures to street addresses of cases and controls reported a nearly five-fold increase in risk of Leukemia among children who resided on streets with the highest traffic density scores compared to those residing in the lowest as discussed by Savitz [28]. Our results show about 49 % of child was lived in countryside and 51 % in modern cities of Libya.

4. Conclusion

The risk factors play an important role in increasing the incidence of leukemia however, the contribution of these factors participating as complementary to each other instead of each factor alone. First and foremost, future studies of childhood leukemia will require more large-scale population in order for the data to be significant and effective. Each risk factor should be investigated separately. Doctors, nurses, pharmacists and scientists are working together around the world to continue to improve outcome for children diagnosed with pediatric cancer.

References


[23] By Daniel J. DeNoon WebMD Health News June 2, 2005


