ORIGINAL ARTICLE

Risk factors of Leukaemia in different hospitals of Punjab

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Abstract

Objective: To investigate potential risk factors of leukaemia.

Method: This case-control study was conducted in 5 hospitals in the province of Punjab, Pakistan, from May to September 2014, and comprised adult leukaemia patients and healthy controls with similar gender and marital status, and children patients and healthy controls with matching age and gender. Interviews were carried out face-to-face with adults and with the parents of the minors to obtain information on family history, lifestyle risk factors, employment history, residential history, trauma history and occupational and non-occupational exposures by using a close-ended questionnaire. Data was analysed using SPSS 16.

Results: Of the 75 adults, 25(33.3%) were patients and 50(66.6%) were controls, while of the 120 children, 40(33.3%) were patients and 80(66.6%) were controls. Among adults those at risk of leukaemia had exposure to chemical factory ($p < 0.05$),positive family history of leukaemia ($p < 0.006$), positive trauma history ($p < 0.004$), those who dyed hair ($p < 0.003$), smokers ($p < 0.054$) were born 1st or 4th among their siblings ($p < 0.037$), lived near crops ($p < 0.069$), worked in oil-refining factory ($p < 0.12$), or spent more than 7 hours under direct sunlight ($p < 0.002$). Among children subjects those at a greater risk of leukaemia had a positive trauma history ($p < 0.000$) who were born 1stor 4th among their siblings ($p < 0.028$), and had a positive family history of leukaemia ($p < 0.0484$).

Conclusion: Knowledge of particular risk factors can help plan and execute safety measures to reduce potentially harmful exposures and decrease risk of leukaemia.

Keywords: Case control study, Leukaemia, Risk factors. (JPMA 68: 857; 2018)

Introduction

Leukaemia is a form of cancer that targets the blood. Leukaemia is caused when control is disturbed over white blood cells' (WBC) lifecycle. WBCs start to die when their number gets higher than other blood cells in a patient's body.[1] Types of leukaemia are named according to the speed of their progression; acute or chronic. The type of leukaemia that develops rapidly is called the acute leukaemia which is caused when the leukaemia cell count increases readily and these abnormal cells cannot perform the functions of regular WBC. Chronic leukaemia is a rather slow developing one. If not treated timely the abnormal cells of leukaemia force the regular blood cells out. Bone marrow test in both these conditions show higher levels of abnormal cells than normal cells. Leukaemia can also be classified by the type of WBC they target; myeloid and lymphoid. Leukaemia hitting myeloid WBC is also called myelogenous or myeloblastic and the one hitting lymphoid type of WBC is also referred to as lymphocytic or lymphoblastic. Lymphoid leukaemia cells may also deposit in the lymph nodes and cause swelling.[2]

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The hematopoietic cell passes through different stages of development to become a specialised cell in order to perform specific functions. First the haematopoietic cell becomes a blast cell which further matures and develops to become the specialised one.

Leukaemia starts developing when the hematopoietic cell transforms into the blast cell and undergoes mutation. It looks like a normal blast cell but cannot perform the normal functions. So it becomes stuck in the immature blast stage and is unable to move further to developmental stages. The problem that causes this stoppage occurs inside the nucleus of the cell where one of the genes or segments of the deoxyribonucleic acid (DNA) become mutated. Usually, this gene is very important for helping the cell mature but once it is mutated, it stops working the way it should. The first thing that happens in leukaemia sufferers is that the blast cells fail to mature normally. Then this cell acquires another mutation and this time it occurs in the gene which is really important for controlling the cell division. This disturbance causes these cells to lose track of number of times they divide and eventually these cells start piling up inside the body.

The normal cells inside the bone marrow constantly compete for space, nutrients and growth factors but these leukaemic cells divide so rapidly that they consume

all the resources making the compensation mechanism impossible.

In addition to this, the process of apoptosis is also impaired which could have been able to control the spread of these leukaemic cells. These are the reasons why the blood study shows decreased amount of red blood cells (RBC), platelets and WBCs.[3]

Factors which can potentially increase the chances of a person to get attacked by this disease include exposure to radiation or carcinogens even if it is controlled and is being used to treat cancer, exposure to benzene most commonly found in petroleum products and cigarette smoke and chemotherapies. Apart from these situational factors some inherent factors can also contribute to the chances, like genetically-acquired diseases of Down's syndrome and ethnicity. Age can also play a vital role in cases of leukaemia.

The signs and symptoms of leukaemia include continuous feeling of tiredness, shortness of breath, pale skin, mild fever or night sweats, bruises for no clear reasons, slow healing of cuts and bruises, pinhead sized red spots under the skin, persistent aches in joints and low white cell counts especially the monocytes and neutrophils. Blood test, bone marrow aspiration and bone marrow biopsy are all established methods to diagnose leukaemia. Blood test shows high or low levels of WBC and shows the presence of leukaemia cells in the blood. Platelet and RBC counts may appear low in few cases. Bone marrow biopsy and aspirations are often done to confirm the diagnosis. These tests also identify the type of leukaemic cells.[4]

Apart from addressing the symptoms of leukaemia, medical treatment is designed to cure the disease as well which includes chemotherapy, interferon therapy and in certain cases a designated monoclonal antibody is also used to treat leukaemia. Although radiation therapy carries considerable side effects but it may also be used for treatment. As a complementary treatment, stem cell transplantation is also used.[1] Primary prevention of leukaemia is possible by prophylactic measures like by avoiding exposure to known risk factors associated with leukaemia such as smoking, benzene exposure and high dose ionizing radiation.[5]

The American Cancer Society (ACS) estimated that about 31,500 individuals in the United States are diagnosed with leukaemia every year and about 21,500 patients die of this disease.[6] The incidence of acute leukaemia is the highest in the United States, Australia, western Europe and even worldwide.[6]

According to a study conducted across five continents, the incidence rate of American males was higher than reported for males in all other continents which implies that incidence rate is higher in white males.[7] Epidemiological studies of acute leukaemia in children have found a number of possible risk factors including environmental, genetic, or infections spread. Only one environmental risk factor, ionizing radiation, has been significantly linked with either acute lymphoblastic leukaemia (ALL) or acute myelogenous leukaemia (AML).[8]

Study conducted in different states of America revealed that maternal age was associated with a linear increase in the risk of childhood cancers overall of 8% per 5-year increment.[9] A study conducted to check the association between residential proximity to agricultural pesticide applications and development of leukaemia showed elevated leukaemia risk association with lifetime moderate exposure, but not high exposure, to certain physicochemical categories of pesticides.[10]

A study was conducted to show the risk of leukaemia due to ionizing radiation of computed tomography (CT) scan. It was found that there was a potential cancer risk from ionizing radiation, in particular for children who are more radiosensitive than adults.[11] In a study conducted in north Germany, among 430 cases, 64 percent had lived lifetime in the vicinity (20 km) of nuclear power plant in operation.[12] A meta-analysis conducted found no strong evidence of a marked increase in the risk of cancer among personal hair dye users.[13] Another study conducted showed causal relationship between high mounting exposure and leukaemia among rubber industry workers.[14]

The current study was planned to assess how consistent the risk factors were with respect to previous studies and which ones of those have causal relationship with leukaemia in adults as well as children.

Subjects and Methods

This hospital-based case-control study was conducted in 5 hospitals in the province of Punjab, Pakistan, from May to September 2014, and, using convenient sampling method, comprised leukaemia patients and healthy controls. Patients recruited were suffering from leukaemia during the time of the study and were confirmed by bone marrow biopsy, while the controls were recruited after their test results showed a healthy

blood picture. Adult patients and controls were selected with similar gender and marital status while children patients and controls were matched according to their age and gender. Interviews were carried out face-to-face with adults and with the parents of the minors to obtain information on family history, lifestyle risk factors, employment history, residential history, trauma history and occupational and non-occupational exposures by using a closed ended questionnaire. Exposure of more than 10 years with more than 48 hours in a week was counted for chemical and radiation exposure. No genetic analysis was done. The data was analysed using SPSS 16. Odds ratio (OR) and 95% confidence interval (CI) were calculated for different exposures using Epi info 7.

Results

Of the 75 adults, 25(33.3%) were patients and 50(66.6%) were controls, while of the 120 children, 40(33.3%) were patients and 80(66.6%) were controls. Adult subjects were at risk of leukaemia if they had exposure to chemical factory ($p < 0.05$),positive family history of leukaemia ($p < 0.006$), positive trauma history ($p < 0.004$), those who dyed hair ($p < 0.003$), smokers(p

Table-1: Adult patients and controls.

	Exposure	Cases (25)	Control (50)	Odds Ratio	Confidence Interval	P value
1	Hair dye	16	15	4.14	1.28-4.95	0.003
2	Smoking	14	18	2.26	0.89-3.25	0.054
3	1st or 4th born among siblings	13	15	2.53	0.968-3.41	0.037
4	Trauma history positive	10	6	4.89	1.378-4.358	0.004
5	Family history of leukaemia positive	8	4	5.41	1.397-4.369	0.006
6	Live near crops	12	15	2.153	0.876-3.07	0.069
7	Live in radiation area	5	8	1.31	0.548-2.5911	0.335
8	Spend >7hrs in front of the sun	16	14	4.57	1.36-5.23	0.002
9	Work in atomic nuclear power	0	3	0	Undefined-undefined	0.145
10	Work in oil refining factory	3	2	3.27	0.862-4.227	0.121
11	Detergent factory	3	0	Undefined	2.310-4.636	0.017
12	Pesticide factory	2	0	Undefined	2.2631-4.451	0.054
13	Pesticide or herbicide shops	1	0	Undefined	2.219-4.28	0.1666
14	Fields	4	6	1.39	0.536-2.858	0.319
15	Cotton or polyester factory	0	0	Undefined	Undefined-undefined	0.554
16	Sugar mill	1	0	Undefined	2.2192-4.284	0.1667
17	Chemical factory	3	1	6.68	1.246-4.701	0.057

Table-2: Child patients and controls.

	Exposure	Cases (40)	Control(80)	Odds Ratio	Confidence Interval	P value
1	Hair dye	26	23	4.603	1.57-4.609	0.00009
2	Smoking	13	19	1.546	0.784-2.235	0.159
3	1st or 4th born among siblings	23	31	2.138	0.989-2.763	0.0281
4	Trauma history positive	20	9	7.889	1.986-4.959	0.000003
5	Family history positive	8	7	2.607	1.005-3.047	0.0484
6	Live near crops	25	39	1.752	0.858-2.478	0.081
7	Live in radiation area	18	10	5.727	1.702-4.247	0.00007
8	Spend >7hr in front of sun	9	20	0.871	0.493-1.682	0.389
9	Work in atomic nuclear factory	1	1	2.026	0.369-6.194	0.333
10	Work in oil refining factory	0	0	0.000	Undefined	0.336
11	Detergent factory	0	2	0.000	Undefined	0.221
12	Pesticide factory	2	3	1.351	0.401-3.653	0.373
13	Pesticide or herbicide shop	5	2	5.571	1.339-3.971	0.023
14	Fields	15	16	2.400	1.052-2.819	0.023
15	Cotton or polyester factory	4	1	8.78	1.53-4.28	0.023
16	Sugar mill	1	1	2.026	0.369-6.19	0.333
17	Chemical factory	3	1	6.405	1.258-4.394	0.059

<0.054),who were born 1st or 4th among their sibling (p <0.037), who lived near crops (p <0.069), worked in oil-refining factory (p <0.12), and those who spent more than 7 hours under direct sunlight (p <0.002) (Table-1). Among children subjects, those at a greater risk of leukaemia were those who had a positive trauma history (p <0.000), who were born 1st or 4th among their siblings (p<0.028), or had positive family history of leukaemia (p<0.0484) (Table-2).

Discussion

The significant difference in one of this study's parameter, hair dye usage, implies a strong association between use of the dye and increased risk of leukaemia. In contrast, a meta-analysis found no strong evidence of such an increased risk.[13]

An Etude Sur les Cancerset les Leucémies de l'Enfant (ESCALE) study conducted in 2007 concluded that there is no familial susceptibility to childhood leukaemia.[15] This conclusion supports the results of this study (p<0.04).

A meta-analysis conducted on the studies from 1970 to 1992 showed a causal relationship between smoking and leukaemia. A systematic review conducted to know the risk factors of childhood leukaemia did not prove smoking to be a strong factor in developing leukaemia in children.[8] Same results are evident from this study that smoking has no significant causal relationship between them.

Similarly, a systematic review was conducted for the decade 1993 to 2002 in 2006 to know the effect of solar ultraviolet (UV) exposure. The results compiled from the strong previous data showed no significant evidence in developing leukaemia in particular.[16] Contrary to that, the result of this study found it to be a significant risk factor.

A systematic review and meta-analysis of childhood leukaemia and parental occupational pesticide exposure showed weaker and less consistent association.[17] However, the results of this study contradict that analysis by showing a strong association.

A pooled analysis done for 5 states of America concluded that there is increased risk of leukaemia with increasing birth order[18] and this study also justifies the claimed causal relationship. However, this study concludes that the children born 1st and 4th among their siblings are significantly at a higher risk of leukaemia.

It is recommended that for all who have already developed leukaemia, their treatment protocol should be established keeping in mind the risk factors to which they are exposed.

For the ones who have not developed leukaemia but are exposed to the risk factors somehow, awareness should be programmed at each and every level which covers every aspect.

Specific safety measures should be taken for the ones exposed with radiation or harmful carcinogens at their work places, employers should be given awareness about it and they should provide their employees with best precautionary measures. Ones who are exposed due to personal carelessness, they should be given proper counselling at hospitals and special seminars should be conducted. To further explore the causes of all types of leukaemia and develop preventive methods for this disease, more in-depth studies are needed.

As the study was not conducted blinded; researcher bias may have affected the results, similarly cases and controls might have answered incorrectly due to their biases, and that may have also affected the results.

Conclusion

Family history of cancer, exposure to carcinogens, born 1st or 4th among siblings, use of hair dye and living near sources of radiation or near crops and a history of trauma were the factors that played a significant role in causing leukaemia. Knowledge of these particular risk factors can help in planning and executing safety measures to reduce potentially harmful exposures and to decrease risk of this disease.

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