

Nutritional Background & BCG Scar Status in Children with Malignant Disease

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ABSTRACT

The causes of most childhood cancer are largely unknown. The causal mechanisms for cancer in childhood as in adult involve an interaction of exposure with inherent genetic susceptibility. Prevention of cancer could avoid 80% of new cases. Immune system plays an important role in the defense mechanism against disease including cancer. BCG scar can be a good indicator for immune response. It is so important to determine the state of immunity in children prior to development of cancer as indicated by their response to BCG vaccination and to determine the nutritional background and their relation to BCG scar size. A case-control study was designed for these objectives. The total patient numbers were 120 cancer cases. Their controls were randomly selected from their neighbors matched for age and sex.

The study shows that negative BCG scars (diameters<1mm) are significantly more detected among cancer cases. And risk of cancer is more in children who are born with body weight of more than 4 kg. Delayed introduction of complementary diet and delayed weaning are associated with reduction in risk of cancer. A significant reverse linear correlation is found between weight at birth and the diameter of BCG scars. While significant positive correlation is found between age at diet introduction and diameters of BCG scars.

So it is advisable to avoid early introduction of complementary diet within the first year of age and to delay weaning to the age of 2 years. The BCG scar can be a good indicator for the integrity of the immune system. It may be a worthy trial to revaccinate individuals for enhancement of immunity in children.

Key words: BCG, nutritional background, scar, cancer

INTRODUCTION

Because of the still limited success of cancer therapy, prevention should be the main concern. Prevention could avoid 80% of cancers. ⁽¹⁾ Although genetic inheritance influences the risk of cancer, most of the variation in cancer risk across populations and among individuals is due to factors that are not inherited. ⁽²⁾ The modulation of the environmental factors by host susceptibility has rarely been evaluated. ⁽³⁾ The scientific study of nutrition and cancer is highly complex, and many important questions remain unanswered. ⁽²⁾ Overweight and obesity are leading nutrition-related disorders of clinical and health concern.

The prevalence of obesity is increasing worldwide. It is emerging as one of the most important contributors to malignant disease. ⁽⁴⁾ The cause of most childhood cancer is largely unknown. Several studies have identified high birth weight (generally defined as > 4000gm) as a risk factor for some types of childhood cancer. ⁽⁵⁾ Immune system plays an important role in the defense mechanism against disease including cancer. ^(6, 7) Generally the immune system is much better at recognizing germs than cancer cells. In contrast to the germs, differences between normal cells and cancer cells may be not clear-cut. ⁽⁸⁾

Patients with immunological disorders and immune deficiency disorders are predisposed to malignant disease. ⁽⁹⁾ Immune-deficient patients following renal transplantation may have a 100-fold increase in risk of cancer. ⁽¹⁰⁾ Immunotherapy is treatment that uses certain parts of the immune system to fight disease, including cancer. This can include stimulating the immune system to work harder, or using an outside source like manmade immune system proteins. ⁽⁸⁾

BCG is a bacterium that is related to the germ that causes tuberculosis. It activates the immune system. The effect of BCG infection on the immune system makes this bacterium useful as a form of anticancer immunotherapy. ⁽¹¹⁾ It is routinely used in treatment of superficial bladder cancer. Researchers are looking at injecting BCG to give an added boost to the immune system when using chemotherapy, radiation therapy, or other types of immunotherapy. ^(6, 7) There is good evidence that a correlation is found between low immunity and poor nutritional habits with the development of cancer. ⁽⁷⁾ BCG scar can be a good indicator for immune response. ⁽¹¹⁾

The objectives of the study are to determine the state of immunity in children prior to development of cancer as indicated by their response to BCG vaccination and other

factors that affect immunity like nutritional status, and also to test the efficacy of BCG vaccination in prevention of cancer.

MATERIALS & METHODS

A case – control study was designed for the given objectives. The study included all of the children with cancer who attended to Basrah Oncology Center at Al-Sadar Teaching Hospital for the period from September 2001 to June 2003. The total patient numbers were 120 cancer cases. Children below one year old were excluded. For each case, one control child was selected from their neighbors matched for age, sex, and hence place of residence (by selecting the best match from the right side neighbor, if no matched pair was available then the left side neighbor was approached, then next right, next left, etc.).⁽¹²⁾

The cancer cases were divided into 3 groups according to the state of their BCG scar size and the nutritional parameters (weight at birth, type of feeding, date of introduction of complementary diet and age at weaning). The diameters of BCG scars were measured by tape measure. And hence the children were divided into the following groups⁽¹¹⁾:

1. BCG positive: scar diameter (> 5 mm).
2. BCG weak positive: scar diameter (1-5 mm)
3. BCG Negative: scar diameter (none or dot like).

For the study of correlation, the number of cases and controls are gathered (total number=240). Statistical analysis was done on SPSS program & $P < 0.05$ was considered as significant.

RESULTS

The total number of children with cancer is 120 cases. Of them, 55.8% is below 5 year old and 66.3% is males (table 1 &2, respectively). The most leading cause of cancer is leukemia followed by lymphoma, CNS tumor, Wilm's tumor, soft tissue tumors and others (table 3). The negative BCG scars (diameters<1mm) are significantly more commonly detected among cancer cases with 2 times more risk of cancer (table 4).

The risk of cancer is 2.4 times more in children who are born with body weight of more than 4 kg as compared with those who are below 3 kg (table 5). No significant differences have been found in the risk of cancer between cases and controls with respect to type of feeding whether breast, bottle, or mixed type (table 6). Delayed introduction of complementary diet to the age of more than one year old are associated with about 3 times reduction in cancer risk (table 7).

While delayed weaning to more than 18 months old of children are associated with risk reduction of 2 times (table 8). Figure 1

shows a significant reverse linear correlation between weight at birth and the diameter of BCG scars. While figure 2

illustrates that there is a significant positive correlation between age at diet introduction and diameters of BCG scars.

Table (1): Age distribution of the studied cases

Age (years)	N	%
<5	67	55.8
5-12	53	44.2
Total	120	100

Table (2): Sex distribution of the studied cases

Sex	N	%
Males	80	66.3
Females	40	33.7
Total	120	100

Table (3): The distribution of cancer cases according to type of cancer among the studied cases

Diagnosis	N	%
Leukemia	56	46.3
Lymphoma	37	30.5
CNS tumor	10	8.4
Wilm's tumor	7	6.3
Soft tissue tumor	5	4.2
Others	5	4.2
Total	120	100

Table (4): The BCG scar size in children with cancer as compared with their controls.

Controls		Cases		BCG scar reaction (Diameters)
%	N	%	N	
23.3	28	46.7	56	Negative (<1mm)
15.8	19	15.8	19	Weak (1-5mm)
60.9	73	37.5	45	Positive (>5mm)
100	120	100	120	Total

$\chi^2 = 16$ df=2 P<0.001 OR=0.5...95% CI: 0.4 to 0.7

Table (5): The weight at birth of children with cancer as compared with their controls.

Controls		Cases		Weight (kg)
%	N	%	N	
33.3	40	23.3	28	<3
51.7	62	49.2	59	3-4
15	18	27.5	33	>4
100	120	100	120	Total

$\chi^2 = 6.6$ df=2 P<0.05 OR=2.4 95%CI: 1.6 to 3.6

Table (6): The type of feeding of children with cancer as compared with their controls.

Controls		Cases		Feeding type
%	N	%	N	
55.8	67	47.5	57	Breast
23.3	28	21.7	26	Bottle
20.8	25	30.8	37	Mixed
100	120	100	120	Total

$\chi^2 = 3.2$ df=2 P>0.05

Table (7): The age at introduction of complementary diet in children with cancer as compared with their controls.

Controls		Cases		Age at diet introduction (mo.)
%	N	%	N	
24.2	29	68.3	82	<6
49.2	59	24.2	29	6-12
26.6	32	7.5	9	>12
100	120	100	120	Total

$\chi^2 = 48.4$ df=2 P<0.001 OR=0.34 CI:0.2 to 0.5

Table (8): The weaning age of children with cancer as compared with their controls.

Controls		Cases		Weaning age (months)
%	N	%	N	
10	12	32.5	39	<12
34.2	41	52.5	63	12-18
55.8	67	15	18	>18
100	120	100	120	Total

$\chi^2 = 47.2$ df=2 P<0.001 OR=0.5 CI: 0.3 to 0.7

Figure 1: The correlation between weight at birth and BCG scar diameter

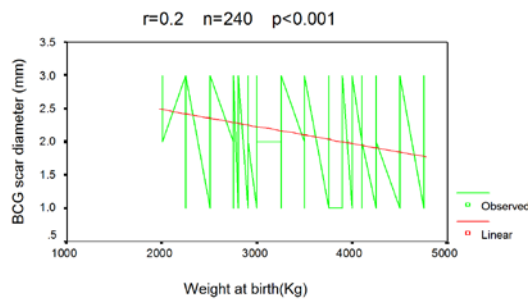
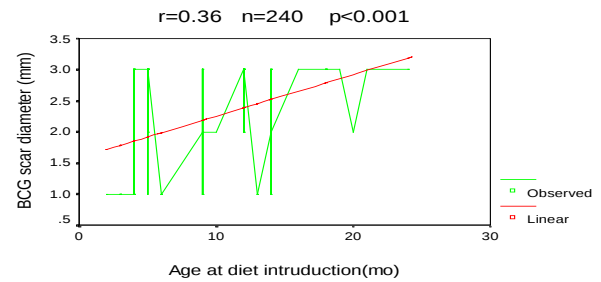


Figure 2: The correlation between age at diet introduction and BCG scar diameter



DISCUSSION

The causal mechanisms for cancer in childhood as in adult involve an interaction of exposure (exogenous or endogenous) with inherent genetic susceptibility, and chance.⁽¹³⁾ The nutritional parameters like weight at birth, type of feeding, age at introduction of complementary diet, and weaning age are important determinants in the growth and development of children. The immune system is one of the most important systems, which develop early in life and depend mainly on the status of these parameters. The distribution of cancer cases according to age, sex and type of cancer is similar to what it is reported worldwide. ^(14, 15)

BCG vaccination is routinely done within the first month of age and the scar usually develops within 6 weeks after vaccination. So that after one year old all the children should have vaccinated and the scars developed. ⁽¹¹⁾

For this reason and for the possible effect of cancer on the development of scars, cancer cases below one year was excluded. The higher percentage of negative scars among cancer cases as compared with their controls can only be explained by abnormal or low level of immunity among them prior to the development of cancer. So that the children with negative scars carry 2 times more risk of cancer as compared with those who have positive scars.

The study demonstrates that cancer is more common in children who were born with high body weight. This finding is similar to what was detected in other study ⁽⁵⁾, but this study also finds that cancer is less common among children who were born with low birth weight (<3kg). Low birth weight is usually associated with negative energy balance and low level of growth factors, which are considered as risk factors like insulin and growth hormone.

They are also more vulnerable to recurrent infection in infancy and early childhood, which is very important for modulating of the immune system. The “delayed infection” hypothesis suggests that leukemia in children is caused by a lack of exposure to infection and a failure of the immune system modulation in infancy, later, an abnormal immune response occurs to delayed infections. ⁽¹³⁾ This may explain the reverse correlation between the weight at birth and the diameter of BCG scars.

For this reason, children with low birth weight present with high percentage of positive scars that may indicate higher level of immunity.

Breast-feeding does not significantly different from bottle-feeding with respect to risk of cancer between cases and controls. Breast-feeding may help prevent childhood overweight, but most studies that examined the relationship of breast-feeding to subsequent obesity failed to find a significant effect. ⁽¹⁶⁾

The effect of bottle-feeding may be reduced by the under-nutrition caused by the expensive and limited amount of the formula. But the early introduction of diet is associated with risk increment of tree times.

The age at diet introduction is directly correlated with the diameters of BCG scars. This may be related to over-nutrition and stimulation of growth factors. It may also be confounded by the weight at birth or the age at weaning where it is found to be correlated and for example early introduction of diet may be followed by early weaning. Giving only three widely separated intervals reduced the recall bias, which is expected especially in regard to birth weight and time of weaning.

CONCLUSION

In conclusion, it is advisable to avoid early introduction of complementary diet and to delay weaning to the age of 2 years. The study also illustrates that BCG scar can be used as an indicator for the integrity of the immune system, and hence the use of BCG vaccination for prevention of cancer. It may be a worthy trial to revaccinate individuals for enhancement of immunity.

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