

# Seroprevalence of EBV in children with acute lymphoblastic leukemia

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## Abstract:

Acute lymphoblastic leukemia (ALL) accounts for about 25 percent of all childhood cancers and 75–85 % of all childhood leukemias. Thirty six children with acute lymphoblastic leukaemia were tested for antibodies to Epstein-Barr (EBV) virus with age ranged (2-12) years (20 males and 16 females) attending pediatric central hospital, oncology-hematology department. Thirty children with age ranged (2-12) years were regarded as control group. The two groups undergo Epstein-Barr virus antibodies assays (EBV-EA IgG, IgM, EBV-VCA IgG, and IgM) by enzyme linked immunosorbent assay (ELISA). The samples analysis was observed that the percentage of VCA-IgG (44.4%), VCA IgM (2.7%), EA IgG (27.7%) and EA IgM (2.7%) were higher than control group. The mean values of EBV (VCA IgG) in ALL group increase significantly when compared with control group, while no significant difference between ALL and control in the mean values of VCA IgM. There was a significant increase in the mean of EA IgG in ALL than in control group, whereas, no significant differences were noticed in EA IgM between two groups. These results clearly indicated that provide a working hypothesis and some facts on which further investigations of etiology of ALL be planned.

**Keywords:** Acute lymphoblastic leukaemia (ALL), Epstein - Barr virus (EBV), early antigen, viral capsid antigen.

## Introduction:

Cancer is the second leading cause of death in children under 15 years of age. Childhood cancers include a variety of malignant tumors. The world wide incidence is approximately 160,000 cases per year, whereas the average mortality rates is 90,000 (1). Leukemia is diagnosed in about 30 – 34% of all Childhood cancers (2), and the most frequent types are acute lymphoblastic leukemia (ALL) and acute myeloblastic leukemia (AML) are found in children (2). Viruses are associated with tumor development in about 15% of malignancies (3). particularly, the Epstein - Barr virus (EBV) infection which is common all over the world (2). Primary EBV infection can lead to latent or chronic infection resulting in lymphoproliferative diseases and has been associated with haematological malignancies, also associated with B- cell lymphoproliferative disease in immunocompromised patients and bone marrow transplantation (4). The concurrence of EBV infection and acute leukaemia has been rarely reported, however we observed seropositivity to EBV in a number of

acute lymphoblastic leukemia (ALL) in children, (5,6).

### The aim of the study

The aim of the present study was to investigate the association of EBV in children with ALL.

## Material and method:

Thirty six children were included in this study suffering from ALL attending pediatric central hospital oncology-hematology department receiving regular chemotherapy. The diagnosis is made by bone marrow examination and the slides reviewed by two hematologists.

The age of leukemic children range (2-12) years 20 males and 16 females. The bone marrow smears were reviewed to confirm the diagnosis of ALL. The second group included 30 children with age ranged (2-12) years complaining of non-malignant disorders.

Venous blood was withdrawn (2ml of blood) from the ALL group and the control group put in clot activator tubes. The following tests were performed viral capsid antigen (VCA-IgG-VCA-IgM) and early antigen (EA-IgG, EA-IgM) using enzyme linked immunosorbent assay (ELISA). The procedures were done according to manual instruction of the kit of Cortez diagnostics.

These studies were done in hematological unit lab in the

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**Methods of Statistics with Ethical approval**

Statistical analyses were carried out using spss software version 17. Values were reported as the mean standard deviation (SD), and independent sample T-test was used to compare the studied groups.

All statistical tests were 2-tailed p value of <0.05 was considered as statistically significant.

The present study was approved by the human research ethics committee at the pediatrics hospital and informed con-

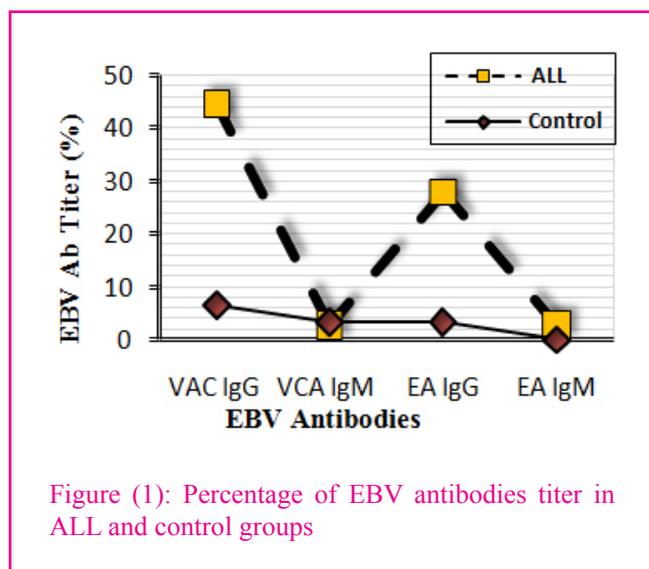
sent was obtained from the parent of each child with leukemia involved in our data.

**Results:**

The results obtained from the serum analysis of children in two groups is presented in (Table 1) and showed in ALL group that the percentage of VCA-IgG (44.4%), VCA IgM (2.7%), EA IgG (27.7%) and EA IgM (2.7%) were higher when compared with the control group ( Fig. 1).

Table (1) The positive cases of EBV antibodies in ALL and control groups

Groups	VCA IgG		VCA IgM		EA IgG		EA IgM	
	No.	%	No.	%	No.	%	No.	%
ALL	16	44.4	1	2.7	10	27.7	1	2.7
Control	2	6.6	1	3.3	1	3.3	0	0



The VCA IgG mean values of EBV in ALL group showed a significant increase ( $P \leq 0.05$ ) when compared with control group, while no significant difference ( $P \leq 0.05$ ) between ALL and control in the mean values of VCA IgM. Whereas, the mean of EA IgG was significant higher ( $P \leq 0.05$ ) in ALL than in control group, whereas, no significant ( $p \leq 0.05$ ) differences were noticed in EA IgM between two groups (Table 2).

Table (2) The mean values of EBV antibodies in ALL and control groups

Groups (Number)	VCA IgG Mean $\pm$ SD*	VCA IgM Mean $\pm$ SD*	EA IgG Mean $\pm$ SD*	EA IgM Mean $\pm$ SD*
ALL (36)	1.2 $\pm$ 0.4 <sup>a</sup>	0.6 $\pm$ 0.3 <sup>a</sup>	1.1 $\pm$ 0.3 <sup>a</sup>	0.4 $\pm$ 0.2 <sup>a</sup>
Control (30)	0.7 $\pm$ 3.2 <sup>b</sup>	0.6 $\pm$ 0.3 <sup>a</sup>	0.7 $\pm$ 0.3 <sup>b</sup>	0.4 $\pm$ 0.3 <sup>a</sup>

Means with same letters within the same column are no significantly differences.

\* SD Standard deviation

## Discussion:

The EBV has been reported as being associated with different malignancies and its role in the carcinogenesis has been proved in some reports (2). However little has published about the association of EBV with acute leukemia, especially in childhood leukemia. We found a significant association between EBV infection and ALL ( $P \leq 0.05$ ) which confirms the previous results by Cader et. al. and Maginnis et. al. (6,7). Associations of EBV with childhood leukemia, mainly lymphoblastic leukemia (ALL), have been found in some seropositivity studies, genetic analyses, and epidemiological studies. One study was shown that EBV viral capsid antigen VCA IgM, in EBV-seropositive mothers, was associated with increased risk of acute ALL and non-ALL in offspring (4). The presence of VCA antibodies is recognized as a sensitive measurement for active infection. While for EBV early antigen antibody was found to be useful tool in diagnosing EBV infection. However, high levels of EBV antibodies in ALL patients who often received blood transfusions, and infection with EBV may be acquired in this way (8,9). In children, it is possible to observe a number of children's with

acute infection and to compare with common latent infection (10). Children with latent infection seemed to be at higher risk of ALL as compared to children with acute infection and (10,11) suggested that latency which occurred between EBV infection and development of malignancy may be due to a multistep process in which the EBV infection represents one of the steps. In children with ALL infected with EBV observed probably due to a weaker cellular immune response to the virus (12).

### Conclusion:

it was proposed that infection maybe triggering mechanism, most probably, the genetic alterations, immunological status and infection has cumulative effect on leukemia development.

Infectious agent is often preventable or treatable therefore, leukemia associated infection may become preventable.

### Recommendations :

Better PCR testing protocols are essential to elucidate the full spectrum of EBV associated with childhood ALL. Improvement of viral therapeutics and development of safe vaccine are recommended to prevent childhood ALL.

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## مدى ظهور ابشتاين بار فايروس في الاطفال المصابين بابيضاض الدم اللمفاوي الحاد

خالد جمعة خليل

المركز العراقي لبحوث السرطان والوراثة الطبية / الجامعة المستنصرية

### الخلاصة:

من المعروف ان ابيضاض الدم اللمفاوي الحاد يشكل 25% من مجمل سرطانات الاطفال و85-75% من ابيضاض الدم لدى الاطفال. تضمنت الدراسة الحالية 36 طفلا مصابين بابيضاض الدم اللمفاوي الحاد تتراوح اعمارهم ما بين (2-12) سنة ومكونة من 20 ذكرا و 16 انثى يراجعون مستشفى الطفل المركزي قسم الأورام وامراض الدم ,ومجموعة السيطرة متمثلة بثلاثون طفلا تتراوح اعمارهم بين (2-12) سنة. تم اخضاع المجموعتين للفحوصات المتعلقة بفايروس ابشتاين بار باستخدام الاليزا لقياس نسبة الاجسام المضادة للفايروس المستضد الابتدائي نوعي جي و أم ( EAIG and IgM ) ومستضد غلاف الفايروس نوعي جي و أم ( VCAIG and IgM ) واطهرت النتائج بان الاجسام المضادة لغلاف الفايروس نوع جي اعلى بفارق معنوي في المصابين مقارنة بمجموعة السيطرة . وهناك فارق معنوي عند الاطفال المصابين في الاجسام المضادة الابتدائية نوع جيم اعلى مقارنة بمجموعة السيطرة . لوحظ ان الاجسام المضادة لابشتاين بار فايروس اكثر انتشارا في الاطفال المصابين مقارنة بالاطفال الاصحاء. بالرغم من ظهور نتائج ذات قيمة احصائية معنوية بين المرضى والاصحاء فان هذه الدراسة استندت الى عدد قليل من المصابين والتي تشكل قاعدة لاجراء بحوث مستقبيلة وعلى اعداد اكبر للحصول على نتائج اكثر عمقا.