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Features of Epstein-Barr virus infection in early childhood

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Abstract

Epstein-Barr Virus (EBV), is a ɣ-herpesvirus, that is ubiquitous in nature and infects most of the people. It causes diseases in human that ranges from mild symptoms that are undifferentiated from other common viruses, to its most common clinical syndrome "Infectious mononucleosis ", to its link with different malignancies and lymphoproliferative syndromes.This study aims to explore epidemiological, clinical and laboratory data of EBV infection in early childhood. There were enrolled 72 children, aged 0-6 years, which resulted infected with EBV, confirmed by serology tests. 2-3 years was the age with the most high number of cases (25%). The most affected gender were males (58%). Fever resulted the most common symptom (98%), followed by sore throat in (65%). Fever duration was approximately 8 days. The most common clinical sigh were pharyngitis (82%), lymphadenitis (75%), splenomegaly (31%), hepatomegaly (27%). Leukocytosis was present in 92% of children, lymphocytosis in 86%. Median time of hospitalization was 9 days. EBV virus can infect children in the first years of life. Its symptoms and signs are similar to other infections of childhood. However the disease appears more severe according to prolongation of the disease compared to other infections in early childhood.

Keywords: EBV; Symptoms; Signs; Infection; Childhood

1. Introduction

The Epstein-Barr virus, a ɣ-herpesvirus is a member of herpes virus family, also known as Herpes Virus 4 according to the sequence of its discovery. It is ubiquitous in nature and causes diseases in humans. The virus is composed by a double helix of deoxyribonucleic acid (DNA) which encodes for 85 genes [1]. The DNA is surrounded by a protein nucleocapsid, the most out layer, the envelope contains both lipids and surface projections of glycoproteins, which are essential to infection of the host cell [2].

Lymphocyte B cells are the main target of infection by EBV, but different cells such as epithelial cells are infected too [3]. The envelope glycoprotein complex gp42 mediates virus entry to B cells, viruses lacking the gp42 portion are unable to infect [4]. After entering the host cell the viral capsid dissolves and the viral genome is transported to the cell nucleus [5]. This process sign the beginning of the lytic cycle of the infection, which results in in the production of infectious virions.

Latency is a characteristic of herpesviruses and EBV is not an exclusion. In latency, the EBV genome resides in the cell nucleus as an episome and is copied by host-cell DNA polymerase [2]. This latent genome persists in the host's memory B cells and can be reactivated to switch to lytic replication [1]. In the early phase of latency B cell is transformed in a proliferating blast, later the virus restrict its gene expression transforming B cell into a memory B cell, however the EBV

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genome to replicate when the memory B cell divides [1, 2]. These memory B cells do not have a normal life span, they continue to divide indefinitely, permitting the virus to persist the whole lifetime of the host [6].

EBV is linked to a wide range of diseases in humans. Infectious mononucleosis is the most common clinical syndrome caused by EBV, specially in children. EBV is the first identified oncogenic virus in humans. The manipulation of the human body's epigenetics by EBV can alter the genome of the cell to the oncogenic phenotypes, this modification increases the host's likelihood of developing EBV-related cancer [7, 8]. EBV is linked to various malignant diseases such as EBV-associated lymphoproliferative diseases such as Burkitt lymphoma, hemophagocytic lymphohistiocytosis, and Hodgkin's lymphoma; non-lymphoid malignancies such as gastric cancer, and nasopharyngeal carcinoma [10,11].

Aim

In this study, there are explored epidemiologic, clinical and laboratory data of EBV infection in early childhood.

2. Material and Method

In the study are enrolled 72 children aged from 0-6 years old. They were hospitalized in the General Pediatric Ward of the University Hospital Center "Mother Teresa", Tirana, Albania during a 4-year period, 2022-2025.

All children were infected by Epstein-Barr virus, confirmed by the presence of IgM-VCA for EBV. There were studied epidemiological, clinical and laboratory features. Data were extracted from clinical records.

3. Results

The age with the most burden of EBV infection in hospitalized children resulted 2-3 years old with 18 children (25%), followed by 1-2 years 15 children (21%), 3-4 years 14 children (19%), 4-5 years 13 children (18%), 5-6 years 10 children (14%), and 0-1 years 2 children (3%) (Figure 1). Of the 72 children, 30 (42%) were males and 42 (58%) were females (Figure 2).

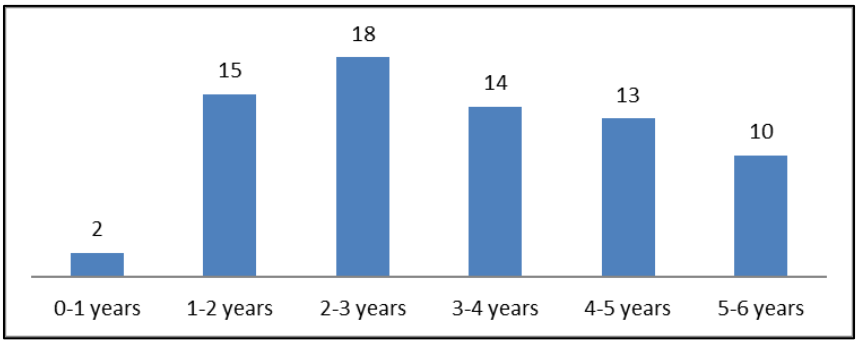

Figure 1 Age distribution of infected children

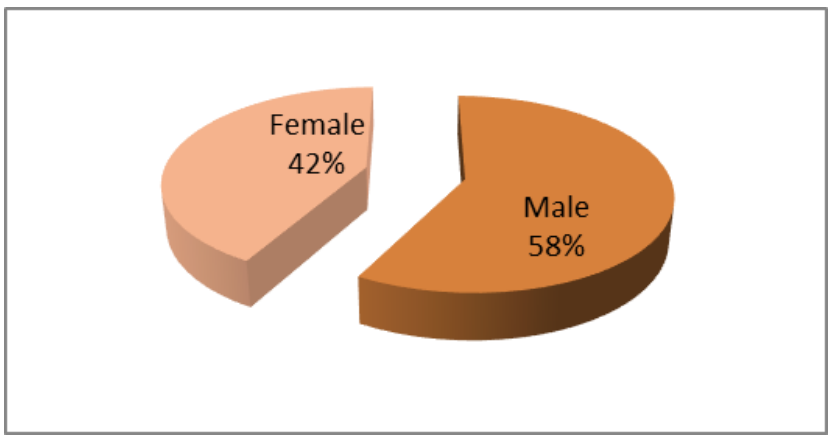

Figure 2 Gender distribution

Fever was the most presenting symptom in 98% of cases, followed by sore throat in 65%, breathing difficulties in 23%, fatigue in 21%, diarrhea in 19%, abdominal pain in 11% and vomiting in 9% of children (Figure 3).

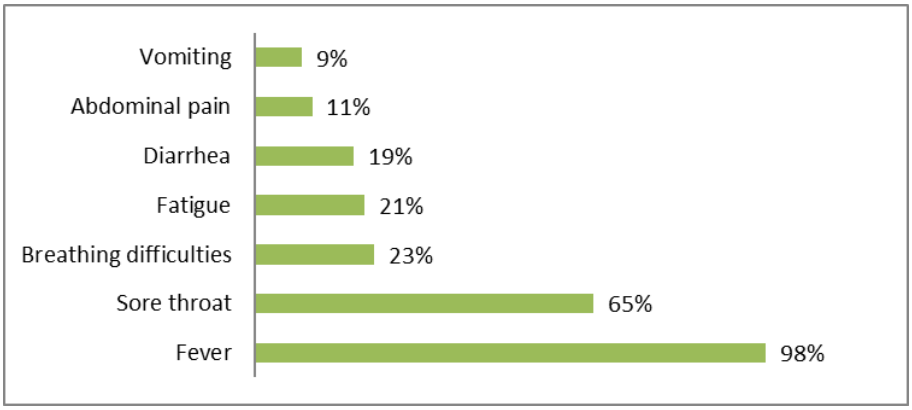

Figure 3 Symptoms of infected children

The most common clinical sign resulted pharyngitis in 82% of children, followed by lymphadenitis in 75%, splenomegaly in 31%, hepatomegaly in 27%, and rash in 14% of children (Figure 4).

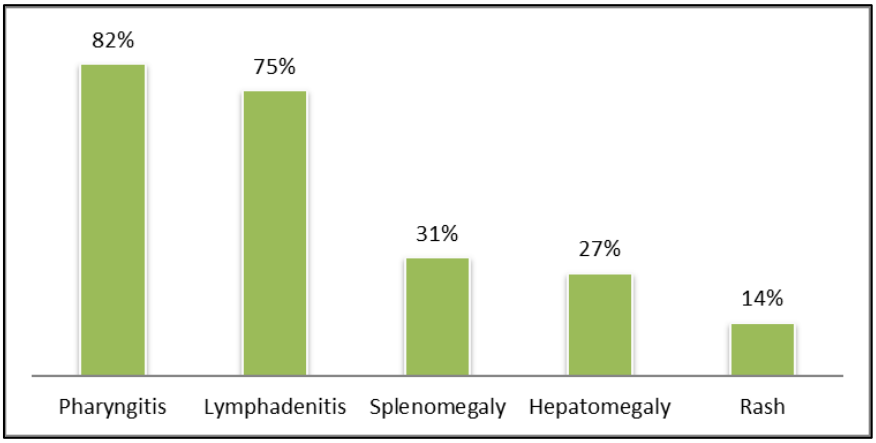

Figure 4 Clinical signs

Laboratory results revealed Leukocytosis (WBC > 10,000 cells/mm^3) in 92% of children, Lymphocytosis (Lymphocytes >50%) in 86% of children, Thrombocytopenia (PLT < 150,000 cells/mm^3) in 10% of children, and elevated level of transaminases (Alanine transaminase ALT > 45 UI/L, Aspartate transaminase AST > 45UI/L) (Figure 5). Normal number of leukocytes were found in 8% of children (WBC 4,000-10,000cells/mm^3), 75% of children displayed moderate leukocytosis (WBC 10,000-20,000cells/mm^3), 17% of children presented with high leukocytosis (WBC >20,000cells/mm^3) (Figure 6).

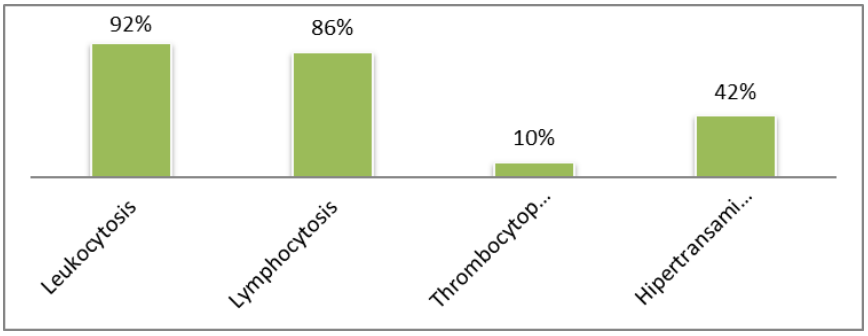

Figure 5 Laboratory findings

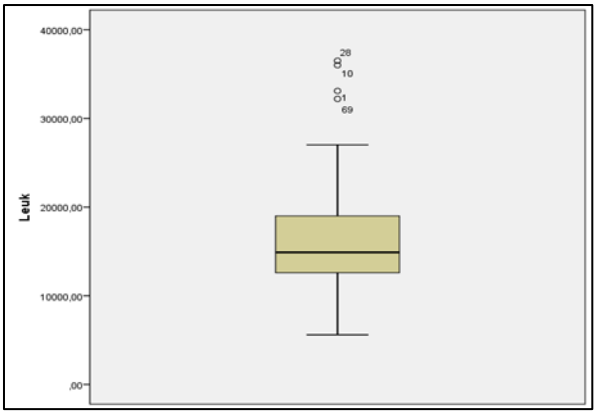

Figure 6 Histogram of leukocytes

4. Discussion

It has been more than six decades, more precisely the 1964, when Sir Michael Anthony Epstein and Yvonne M. Barr, discovered Epstein-Barr virus (EBV) by electron microscopy of suspension cultures of African Burkitt lymphoma cells. Four years later, in 1968 Henle reported the link between EBV and Infectious Mononucleosis, which is its most common clinical manifestation [12].

EBV is ubiquitous in nature and its infections occur in all regions of the world. Humans are the only reservoir for EBV, most of the world population is infected by it. The results of this study showed can be infected with EBV at any age, since the first year of life. The age with the greater number of infections was 2-4 years old, it coincides with the time when most children begin to frequent day-care facilities, exposing them to close contact with other children. The main way of transmission of EBV is via exchange of oral secretions, other rare ways of transmission are through blood products and solid organ transplant. In young children that frequent day-care institutions, the close contact and the share of toys, bottles and other person items is the way of transmission. Healthy adults and children continue to shed EBV for many months after their acute infection and are potentially capable of transmitting it [13]. Latency is a feature of EBV , making so possible that infected B cells, are being stimulated to reactivate EBV. This process produces virus that can re-infect new B cells and epithelial cells, becoming so a source of viral transmission [14]. Crowded living conditions are another factor that predispose children to be infected in a younger age.

A potent innate and adaptive immune response occurs during primary EBV infection, which is responsible for most symptoms and signs that accompany the infection. EBV infection is often insidious with nonspecific symptoms as fatigue, body aches, followed by fever, sore throat and swollen of posterior cervical lymph nodes [15, 16]. In the studied children fever was present in almost all children, but other infections of childhood are presented with fever too. Even the other symptoms; sore throat, difficulty in breathing, fatigue and gastro-intestinal symptoms are very common in early childhood infection diseases. IFN-γ is considered to be important for control of EBV infection and reactivation, furthermore high levels of IFN-γ likely contribute to the symptoms experienced during acute infection, as this cytokine is known to cause headache, fatigue, and fever [17,18]. NK cells are another important component of the immune response that play a key role in EBV infection, their number increase during acute infection and are inversely associated with disease severity [19]. This high immune system activation is responsible for the symptoms and signs of EBV infection regarding severity and duration. Hepatitis, reflected by elevation of transaminases, was found in 42% of children. Most studies have discovered hepatic involvement in over 80% of cases, which regard it as a common feature of the disease. The adaptive immune response especially cellular immune responses, is highly activated. Both CD4 and CD8 T cells make a robust response to EBV antigens, early in infection, CD8 T cells specific for lytic antigens tend to dominate the response [20,21]. This large adaptive immune response is thought to be responsible for the major symptoms of infectious mononucleosis, as disease severity correlated more closely with lymphocytosis. This lymphocyte expansion is responsible for the most common signs as pharyngitis, lymphadenitis, spleen and liver enlargement. Mostly of the infected children had increased number of leukocytes (92%), and also a great number (86%) had increased levels of lymphocytes. This highly activation of the innate immunity by EBV leads to prolonged symptoms as fever, which in the studied children resulted in a medium of 8 days, and a prolonged hospitalization (medium 9 days), which is longer than other infections of childhood.

5. Conclusion

EBV can infect children in the first years of life. The most affected are children 2-3 years, time when they share objects. EBV infection is hardly differentiated from other acute infections in early childhood. The most common signs/symptoms are fever, pharyngitis, lymphadenitis. However the duration of symptoms of EBV infection in young children is longer than the other infections.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

Authors declare no conflict of interest.

Statement of informed consent

Informed Consent was taken from the parents of hospitalized children included in the study, for using the data of their medical records, providing anonymity.

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