EIROPAS SAVIENĪBA

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# Presence of active HHV-6, HHV-7 and parvovirus B19 infection/co-infection in patients with chronic fatigue syndrome/myalgic encephalomyelitis

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## Introduction

CFS/ME is a chronic neuro-immune illness defined by combination of non-specific symptoms of uncertain cause and pathogenesis. Immunomodulating viruses (HHV-6, HHV-7, parvovirus B19) are considered as possible trigger factors for CFS/ME development. The aim of this study was to evaluate frequency of HHV-6, HHV-7 and B19 infection activation/co-activation and association with clinical findings in CFS/ME patients.

## Methods

108 patients (71 females and 37 males, mean age 37 years) with clinically diagnosed CFS/ME corresponding to CDC definition criteria were enrolled in the study. Plasma/serum samples were tested for HHV-6 and B19 IgG and IgM antibodies using ELISA. Qualitative and quantitative PCRs were used for viral genomic sequence detection in PBL and cell-free plasma DNA samples.

## Results

HHV-6 specific IgG and IgM antibodies were detected in 81.5% and 14.8% patients, respectively, B19 specific IgG and IgM antibodies – in 73.1% and 26.9% patients, respectively (Fig.1; Fig.2).
Virus specific sequences were detected in 70/108 (64.8%) patients plasma DNA samples, from them single virus sequence – in 41 (38.0%) DNA samples (HHV-6 – 2, HHV-7 – 28, B19 – 11) and double or triple virus sequences – in 29 (27.0%) samples (HHV-6+HHV-7 – 10, HHV-7+B19 – 15, HHV-6+HHV-7+B19 – 4) (Fig. 3).
HHV-6-PBL load was higher in patients with active HHV-6 and HHV-7 co-infection than in patients with single HHV-6 infection (1007.8±367.1x$10^3$, 133.0±10.3x$10^3$, copies/± µg DNA, respectively) (Fig. 4).

Figure 1.
**HHV-6 specific antibodies in patients with chronic fatigue syndrome/myalgic encephalomyelitis**

Figure 2.
**B19-specific antibodies in patients with chronic fatigue syndrome/myalgic encephalomyelitis**

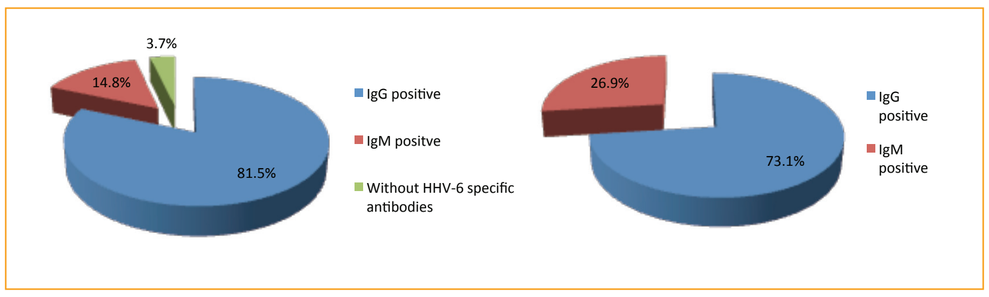



Figure 3.
**Virus specific genomic sequences in plasma DNA samples of patients with chronic fatigue syndrome/myalgic encephalomyelitis**

Figure 4.
**HHV-6 PBL load in patients with active HHV-6 and HHV-7 co-infection and single HHV-6 infection (copies/µg DNA)**

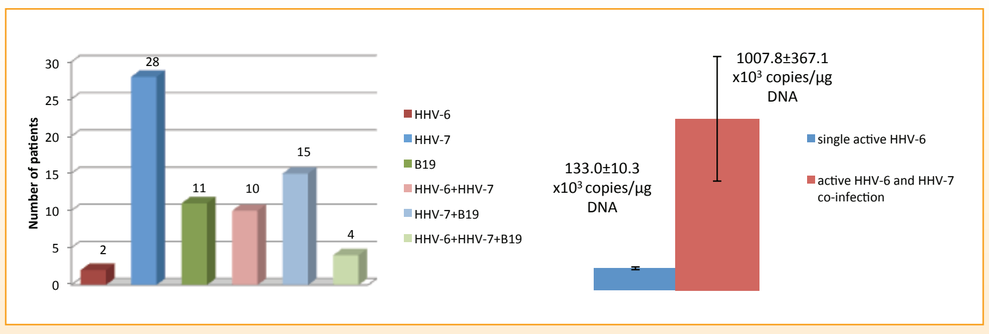
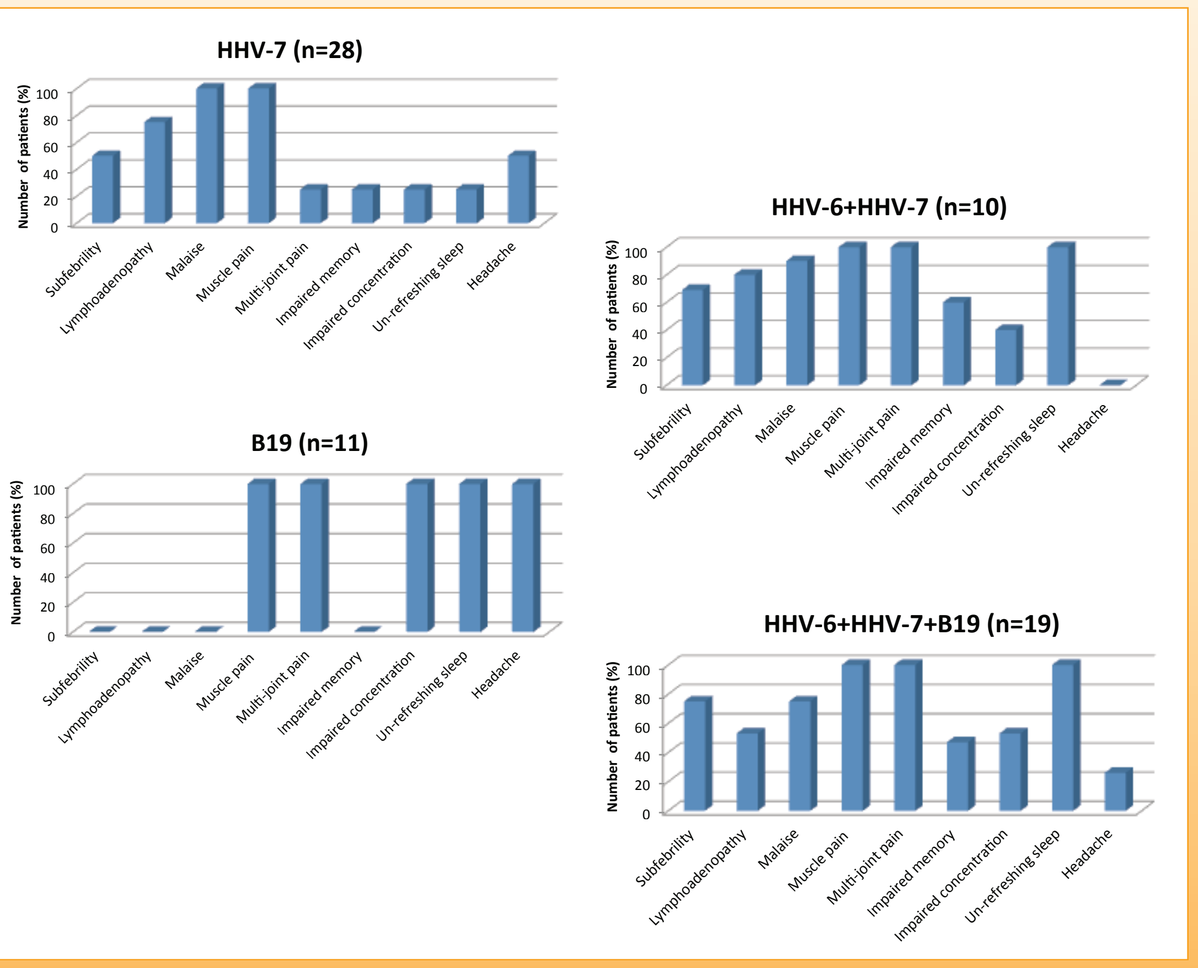



Figure 5.
**An assesment of β-herpesvirus and B19 infection/co-infection activation in CFS/ME patients: association with clinical outcomes**




## Association with clinical outcomes

- Severe chronic fatigue for at least six months or longer was recognized in all patients independently from the causation of the active infection.
- Subfebrility, tender cervical or axillary lymph nodes and post-exertional malaise were not revealed in patients with single B19 infection but were detected in patients with single HHV-7 infection (50.0%, 75.0%, 100%, respectively) and HHV-6+HHV-7 co-infection (70.0%, 80.0%, 90.0%, respectively).
- Persistent muscle pain and muscular weakness were detected in all patients with manifestation more severe in patients with HHV-6, HHV-7 and HHV-6+HHV-7 infection (Fig. 5.).
- Multi-joint pain also was determined in all patients with stronger symptoms in HHV-7+B19 (82.5%) and HHV-6+HHV-7+B19 (100%) co-infection cases.
- Neuropsychological disturbances were detected in all patients: impaired memory – in 85.0% patients with active HHV-7 and HHV-6+HHV-7 infection, and impaired concentration – in all patients with active B19, HHV-7+B19 and HHV-6+HHV-7+B19 infection.
- Un-refreshing sleep was revealed in all patients with sleepiness more characteristic in patients with HHV-7, HHV-6+HHV-7 (87.5%) and HHV-6+HHV-7+B19 infection, and insomnia – in all patients with HHV-6, B19 and HHV-7+B19 infection.
- Headaches of new type were reported from all patients with B19 infection versus 41.7% in patients with HHV-7 and HHV-6+HHV-7 infection.

## Conclusions

High rate of active HHV-6, HHV-7, B19 infection or in combination suggests that each of these immunomodulating pathogens could be a trigger factor for CFS/ME development. The association between the high frequency of active co-infection and the distinctive types of clinical symptoms shows the necessity of a simultaneous study of these viral infections to define possible subsets of CFS/ME.

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