

# EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM Research Protocol

# Erosive Gastroesophageal Reflux Disease: Immunohistochemical Evidence

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#### **Abstract**

This paper investigates the features of erosive gastroesophageal reflux disease (GERD) in patients with persistent herpes simplex virus (HSV) in the esophageal mucosa (EM). We examined 214 patients suffering from erosive GERD. Immunohistochemistry (IHC) was used to identify 79 patients with chronic viral infection. HSV persistence was revealed in 46.3% of patients among whom HSV was detected in 69.7%, cytomegalovirus (CMV) in 58.6% and Epstein-Barr virus (EBV) in 36.4%. Moreover, 37 (37.4%) patients had a combination of different viruses - from 2 to 3 species. The study showed that chronic viral infection of the EM is widespread among patients with erosive GERD.

Keywords: GERD; Erosive Esophagitis; Herpes Simplex Virus; Epstein-Barr Virus; Cytomegalovirus; Immunohistochemistry

#### Introduction

GERD prevalence tends to grow in Russia and in the world [1,2]. Today, it is considered the main cause of erosive esophagitis (EE). However, more and more studies are coming up with evidence suggesting that erosive esophageal ulcers are heterogeneous in nature, in which 65.9% of esophageal erosions and ulcers are attributed to GERD alone [3]. Perhaps, persistent HSV should be considered one of the causes of EE [3-8]. The routes of penetration of viruses into the EM are not yet fully understood. It is assumed that the virus enters the EM from the oropharynx, or along the branches of the vagus nerve upon reactivation of the infection [3-6]. Probably, in this case, chronic, recurrent erosive esophagitis develops. This issue has been most studied in children [7,8]. According to sparse literature, HSV is the most common esophageal viral infection, which is found in 69.1 - 77% of patients with EE [7-10]; CMV is the second most viral infection of the esophagus. HSV and CMV can coexist together or with candidiasis [11]. In this case, the complaints are similar to those of GERD [6,8,10].

The clinical presentation of EE amidst viral persistence in the EM is nonspecific. It includes the same symptoms as GERD - heartburn, chest pain, belching, and nausea [7-10]. Thus, evidence on the role and prevalence of esophageal viral infection in EE cases is scarce and scattered, thus requiring further investigation.

#### Aim of the Study

The aim of this study is to investigate the features of erosive GERD in patients with persistent HSV in the EM.

#### **Materials and Methods**

Endoscopy revealed EE in 214 patients. The examination was performed using video system Olympus Exera II (Japan). All patients underwent esophageal biopsy for morphological examination and immunohistochemistry (IHC) to determine the persistence of herpes viruses (HSV type 1 and 2, Epstein-Barr virus and cytomegalovirus).

#### **Results**

IHC identified chronic viral infection of the EM in 99 (46.3%) patients. Out of these, HSV was detected in 69.7% of patients, CMV in 58.6%, and EBV in 36.4% (Figure 1 and 2). At the same time, 35 (35.4%) patients had a combination of different viruses, from 2 to 3 species at the same time.

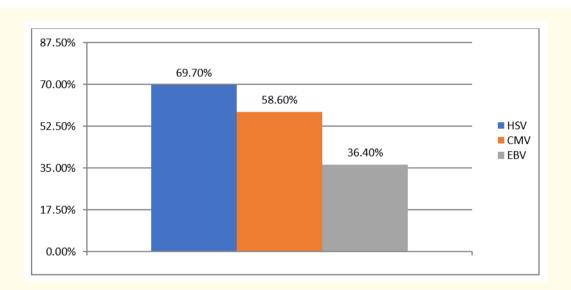


Figure 1: Structure of viruses detected by IHC in the esophageal mucosa (n = 99).

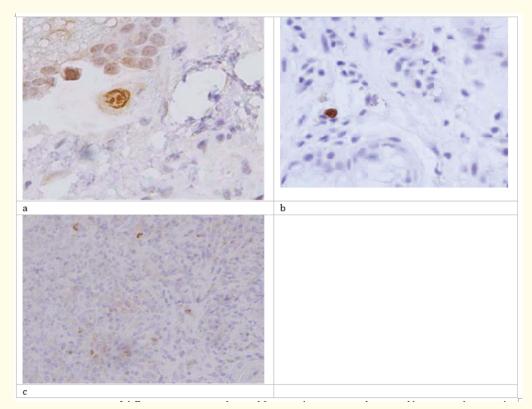


Figure 2: Expression of different virus species detected by IHC. a) Herpes simplex virus; b) Cytomegalovirus; c) Epstein-Barr virus.

#### Discussion

Esophageal chronic viral infection is common in erosive GERD cases. Persistent HSV is detected in 46.3% of patients, which is significantly lower than in children [11]. It should be noted that the structure of detected viruses is consistent with the available literature data [8].

## **Findings**

- 1. There is 43.6% prevalence of chronic viral infection of the esophageal mucosa in erosive GERD cases.
- 2. HSV is relatively most common detected in 69.7% of patients.
- 3. About 35.4% of patients have a combination of several virus species.

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