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Comparative study for children infected and non infected by Roseola Infantum using ELISA technique for detection antibody IgM, IgG in Diyala Province

A thesis

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Chapter One
1. Introduction

1.1.Background:

Human herpes virus type 6 was first isolated in 1986 from the patients with lymphproliferative disorders, using techniques for the culture of the lymphoid cells and then isolated the viruses that infect these cells. The isolation of HHV-6 marked the beginning of an era of discovery in the herpes virology, with the subsequent identification of human herpes virus-7 and human herpes virus-8 during the following decade (Salahuddin *et al*., 1986). HHV-6 is double stranded DNA enveloped with an icosahedral**,** spherical to pleomorphic, capsid composed of 162 capsomeres. Genomes are linear non-segmented, around 200 kb in length (Braun *et al*., 1997).

The virion's outer portion consists of a lipid bilayer membrane that contains viral glycoproteins which is derived from that of the host cell. Like other human herpes viruses, HHV-6 is ubiquitous and capable of establishing a lifelong latent infection of its host particularly the infants and the young children with subsequent viral reactivation in immunocompromised host (Miszczak *et al*., 2013).

The HHV-6 infection was usually acquired very early in the life, between the age six months and two years , following loss of the protective maternal antibodies (Tesini *et al*., 2014). At an even earlier period of life, congenital infection following intrauterine transmission has been reported for about 1% of children, a frequency closed to that observed with Human Cytomegalovirus, and cases of perinatal transmission have been described (Hall *et al*., 2004).

The HHV-6A and HHV-6B were ubiquitous viruses that are detected in all human populations around the world, as reviewed by (Knipe *et al*., 2013). As a whole, HHV-6 infection is detected in more than 90% of adult populations in developed

countries, although the data on seroprevalence may reveal significant differences according to geographic location, age of subjects, sensitivity and specificity of serologic assays.

Roseola infantum is a common disease of childhood caused by a primary infection with HHV-6 and less frequently by HHV-7, and it is also known as exanthema subitum or the sixth disease, because it ranks as the sixth condition following measles, scarlet fever, rubella, Duke's disease and parvovirus B19 in causing skin rash in infants.The classic presentation of roseola infantum is an acutely developed high fever and often a febrile seizure, followed by a rapid defervescence after 3 days and a morbilliform rash appears predominantly among 9 to 12 month-old infant. The fever generally lasts for three to five days and the rash is generally pink and lasts for less than three days (Tesini *et al*., 2014; Arnez *et al*., 2016).

Transmission occurs most frequently through the shedding of viral particles into saliva. Both HHV-6B and HHV-7 are found in human saliva, the former being at a lower frequency. Studies have reported varying rates of prevalence of HHV-6 in saliva between 3% - 90% and have also described the salivary glands as an *in vivo* reservoir for HHV-6 (Suga *et al*., 1998).Vertical transmission was also described, and occurs in approximately 1% of births in the USA (Hall *et al*. 2004*;* Flamand *et al.*, 2010).Direct close contact is required for transmission, supported by the observations that having older siblings and parents who share saliva are associated with virus acquisition (Zerr *et al*.,2005; Rhoads *et al*.,2007). The HHV-6 viral DNA was identified in nasal mucosa and olfactory bulb specimens (Brenda *et al*., 2014).

In the children with primary infection, anti-HHV-6 antibody was detectable from 3–7 days (Dockrell *et al*., 1999). IgM production peaks in the 2nd week and continues detectable for two months after infection. IgG antibodies rise by two weeks post

infection and were detectable for the life in 90% or more of the adults (Yamanishi *et al*., 1988; Robinson, 1994). In contrast, with the children who experienced HHV-7 followed by HHV-6 infection, the IgM response was firstly directed against HHV-6, suggesting that cross-reactive responses to heterologous virus infection (Yoshida *et al*., 2002).

1.2. Aims of the study:

The present study was designed to achieve the following goals:

1. Exploration of the role of HHV-6 as a causative agent for roseola infantum among Diyala children through the detection of anti-HHV6 IgM among clinically suspected cases of roseola infantum.
2. Exploration of the rate of anti-HHV6 IgG among age and sex matched apparently health children.
3. Figure out the effect of socio-demographic risk factors on the rate of infection and their relation with anti-HHV6 antibodies.