Republic of Iraq
Ministry of Higher Education And Scientific Research
University of Dyiala College of Medicine

HERPES SIMPLEX IN PREGNANT WOMEN

A project submi/ed to the council of College of Medicine/University of Dyiala in Partial fulfillment of the Requirements for the Degree of bachelor

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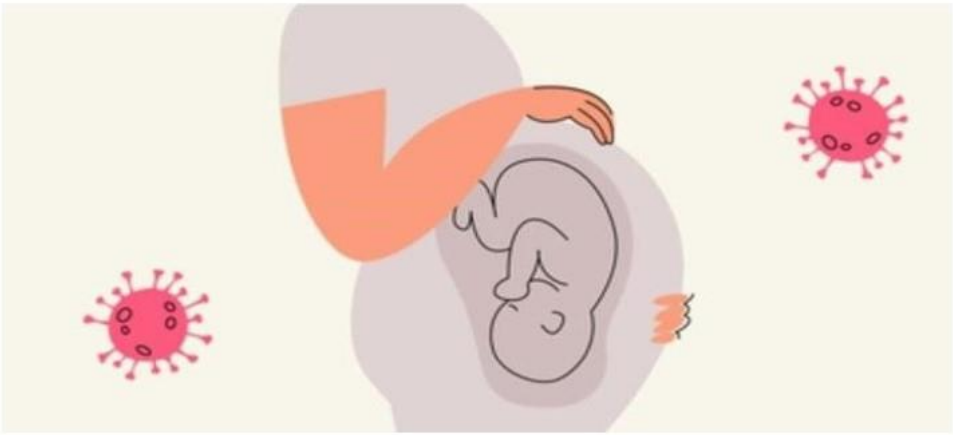

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ABSTRACT

Herpes simplex virus (HSV) infection may lead to severe illness in pregnancy and may be associated with transplacental virus transmission and fetal infection. The consequences may be abortion, stillbirth and congenital malformations. In neonates, the clinical findings after intrauterine HSV infection are characterized by skin lesions, diseases of the eye and neurologic damage. Herpes genitalis of pregnant women at the time of labor may result in life-threatening neonatal herpes. Currently, neither active nor passive immunization is available to prevent HSV infections during pregnancy and in the newborn infant. Therefore, antiviral treatment using aciclovir and/or valaciclovir must be considered in all primary episodes of genital herpes as well as in neonates who show signs of either infection. Clinical herpes lesions of the genitalia and/or positive test for virus detection at the time of delivery are an indication for cesarean section. However,

this surgical intervention may be reduced by suppressive treatment of recurrent genital herpes with aciclovir or valaciclovir.

INTRODUCTION

Herpes simplex virus (HSV) infections of humans were first documented in ancient Greece. Greek scholars, particularly Hippocrates, used the word ‘‘herpes,’’ meaning to creep or crawl, to describe spreading lesions recognized person-to person transmission of HSV infections .Following primary infection, neutralizing antibodies to HSV develop in the serum. Subsequently, some seropositive develop clinically mild recurrent labial or genital lesions, typifying the unique biological property of HSV, namely an ability to recur in the presence of humoral immunity or reactivation of latent infection. The spectrum of disease caused by HSV includes primary and recurrent infections of mucous membranes
(e.g., gingivostomatitis, herpes labialis, and genital HSV infections), keratoconjunctivitis, neonatal HSV infection, visceral HSV infections in immunocompromised hosts, HSV encephalitis, Kaposi’s varicella-like eruption, and an association with erythema multiforme.

HSV STRUCTURE AND REPLICATION

HSV is a member of a family of viruses whose genomes consist of a single large double-stranded DNA molecule .The herpes simplex virion consists of four components: An electrondense core containing viral DNA ,, An icosadeltahedral capsid ,, An amorphous, at times eccentric layer of proteins, designated tegument, which surrounds the capsid; and an envelope.

The capsid consists of 162 capsomeres and is surrounded by the tightly adhering tegument. The envelope surrounds the capsidtegument structure and consists of at least 10 glycosylated and several nonglycosylated viral proteins, lipids, and polyamines. Viral DNA contains at least 152 kbp. The variability in size is due chiefly to the variation in the number of reiterations of specific terminal and internal sequences.

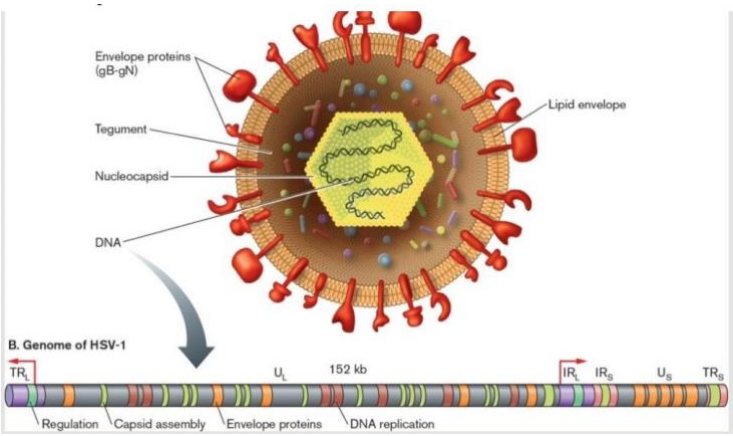

Figure (1) : The structure of HSV

EPIDEMIOLOGY

Although HSV transmitted by different routes and involve different areas of the body, there is an overlap in the epidemiology and clinical manifestations. These viruses are distributed worldwide, and infection occurs in both developed and developing countries. Animal vectors of human HSV infections have not been described, and humans remain the sole reservoir for transmission to other humans. Virus is transmitted from infected to susceptible individuals during close personal contact. There is no seasonal variation in the incidence of infection. Because HSV infection is rarely fatal, and HSV establishes latency, more than one-third of the world's population has recurrent HSV infections and, therefore, the capability of transmitting HSV during episodes of productive infection. Genital HSV infection in pregnant women must be considered separately from that in nonpregnant populations because of the risk to the fetus or newborn.

Transmission of infection to the fetus is related to shedding of virus at the time of delivery. The prevalence of excretion at delivery varies from 0.5% to 1.0% for all women, irrespective of history.

PATHOGENESIS

Primary and recurrent infections result in lesions and inflammation around the genital area and the latter accounts for majority of genital herpes instances. Immunocompromised patients including neonates are susceptible to additional systemic infections including debilitating consequences of nervous system

inflammation. Neonatal herpes simplex virus (HSV) infection is usually acquired at birth. We present an infant with intrauterine HSV infection acquired after rupture of membranes.

CLINICAL MANIFESTATIONS

herpes simplex virus (HSV) infection may lead to severe illness in pregnancy and may be associated with transplacental virus transmission and fetal infection. The consequences may be abortion, stillbirth and congenital malformations. In neonates, the clinical findings after intrauterine HSV infection are characterized by skin lesions, diseases of the eye and neurologic damage. Herpes genitalis of pregnant women at the time of labor may result in life-threatening neonatal herpes The acquisition of genital herpes during pregnancy has been associated with spontaneous abortion, prematurity, and congenital and neonatal herpes..

Herpes can lead to death or long-term disabilities. Rarely in the uterus, it occurs frequently during the transmission delivery. The greatest risk of transmission to the fetus and the newborn occurs in case of an initial maternal infection contracted in the second half of pregnancy

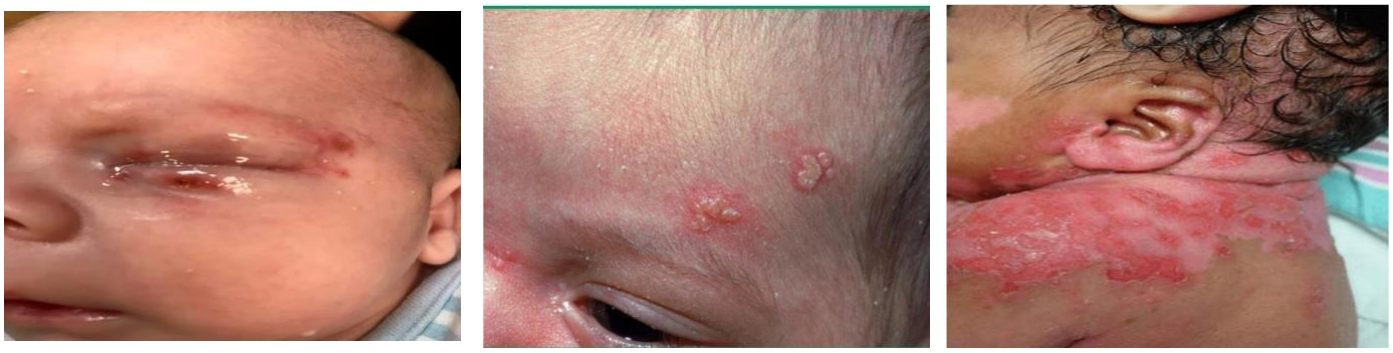

Figure (2) : HSV have been describe a group of vesicles with erythematosus base

DIAGNOSIS

Method	Tissue sampled	Sensitivity	Specificity	Advantages	Disadvantages
Virus isolation by cell culture[1]	Skin/mucosal lesions (stage):				Specialized laboratories
	- vesicular content	>90%		Gold standard	Virus transport medium
	- ulcers	95%	~100%	Simplicity of sampling	Transport rapid, cooled, protected from light
	- scabs	70%		Virus typing	Results in 2/7 days
	- mucosa without lesions	30%		Resistance phenotype determination	Not suitable for CFS
		Unknown			Arrangement with laboratory necessary
	Biopsies				
	Conjunctival smear/corneal				
	Neonates				
Cytologic diagnosis (Tzanck's smear)[35]	Skin/mucosal lesions	73–100%	100%	Easy, quick, reproducible and inexpensive	Optimal lesions are fresh, intact bisters of 1/3 days' duration
	Biopsies				
	Conjunctival smear/corneal				
IF (detection of infected cells)[30]	Smears, tissue sections, smears from base of vesicle	41–70%	>95%	Rapid (<4 h possible) Typing possible	Fresh vesicles
					Specialised laboratories
					Technically demanding
					Not standardized
Virus antigen detection by EIA o ELISA[30]	Smears from lesions, vesicular content with base of vesicle	41–80%	80%	Simplicity of sampling	Suitable only for fresh vesicles
				Does not require the integrity of the specimen	
				Rapid (<4 h possible)	
				Typing possible	

				PCR:	
				Most sensitive method	
Virus DNA detection by **PCR**[30] or **Real-time PCR**[31]	CSF	9798%	~100%	Result within 24–48 h	Only in specialised laboratories
	Aqueous or vitreous humour			Virus typing and resistance genotyping	Not standardised
				Method of choice for CSF	Not validated for all samples
					Risk of contamination (PCR)
				Real-time PCR:	High costs (real-time PCR)
	Skin lesions, vesicular content or mucosa without lesions			Rapid amplification	
				Quantitative analysis	
				Reduced risk of contamination	
				Method of choice for skin lesions	

Table (1) : Methods of diagnosis of HSV

TREATMENT

Mangement according to the type of maternal infection (primary or recurrent) and the gestational age at which infection occurred. The subsequent management of the neonate also reflects the mode of delivery and their condition. New to this guideline are sections on preterm labour rupture of membranes (PPROM) and the management of women who are HIV positive, and a clinical algorithm. In addition, a stronger recommendation to offer vaginal birth to women with a recurrent infection has been made

Mode of delivery

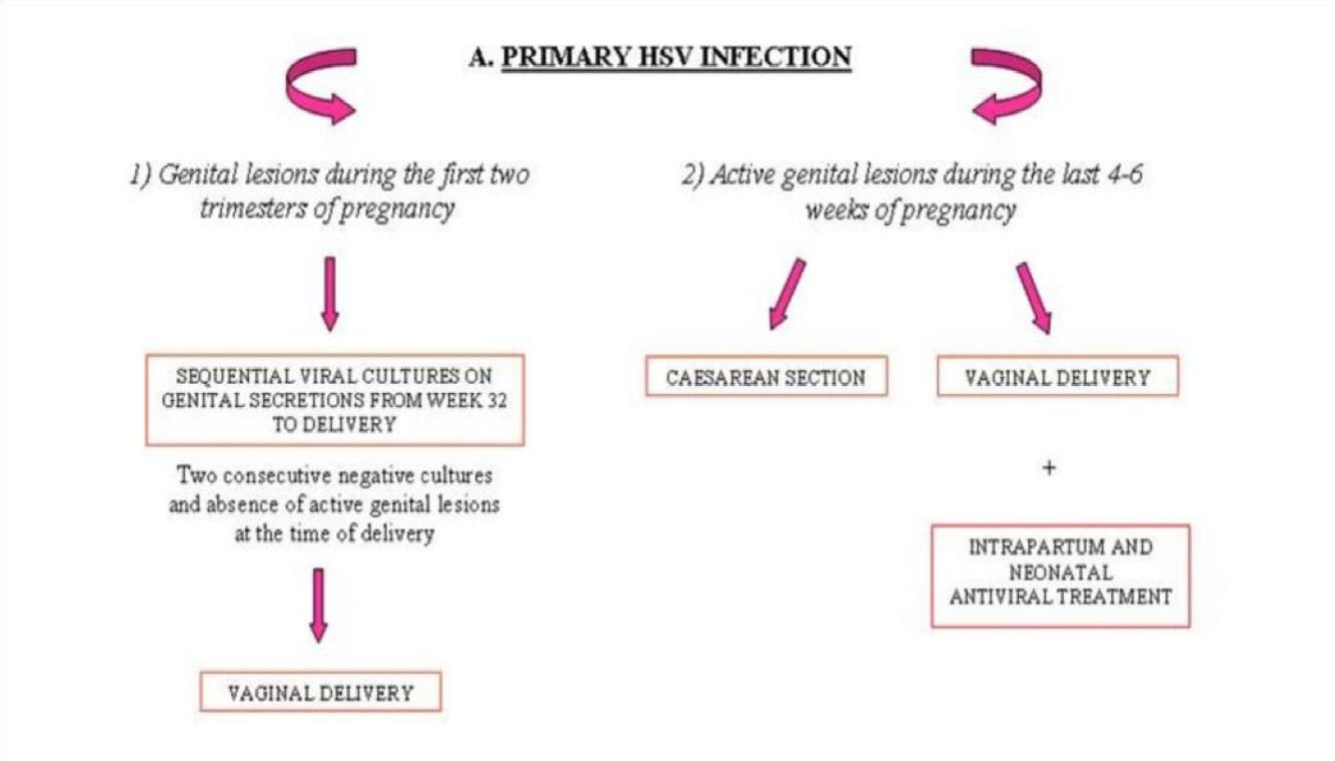

Figure (3) : (A) mode of delivery in case of primary HSV infection

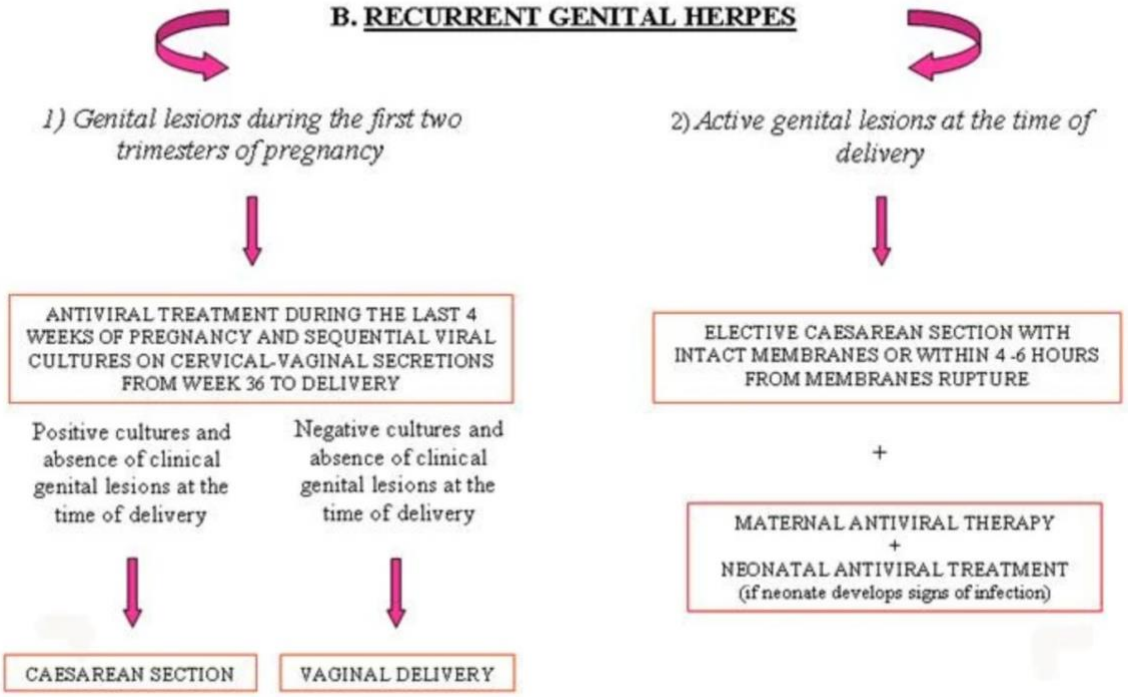

Figure (4) : (B) mode of delivery in case of recurrent genital herpes

Antiviral therapy :

The use of antiviral drugs is allowed before the 36th week in case of very serious events in the mother, or if there is an increased risk of preterm delivery. The therapy includes the administration of acyclovir 400 mg tablets 3 times daily or acyclovir 200 mg tablets 4 times a day from week 36 until delivery, and viral cultures on cervical-vaginal secretions from 36th week of gestation are required. Recent studies also suggest the use of valacyclovir at a dose of 200 mg 2 times a day.

In absence of clinical herpes lesions but with positive viral cultures at delivery, caesarean section is recommended. On the contrary, if all viral cultures are negative, in the absence of clinical lesions, a spontaneous delivery is indicated.

Drug and dose	Frequency	Duration*
Acyclovir, 400 mg	Three times per day	7 to 10 days
Acyclovir, 200 mg	Five times per day	7 to 10 days
Famciclovir (Famvir), 250 mg	Three times per day	7 to 10 days
Valacyclovir (Valtrex), 1 g	Twice per day	7 to 10 days

Table (2) : Antiviral drugs used in the treatment of HSV infection

One of articles

One of studies on 7046 pregnant women whom serologic tests showed to be at risk for herpes simplex virus (HSV) infection. Serum samples obtained at the first prenatal visit, at approximately 16 and 24 weeks, and during labor were tested for antibodies to HSV types 1 and 2 (HSV-1 and HSV-2) by the Western blot assay, and the results were correlated with the occurrence of antenatal genital infections.

Conclusion

Two percent or more of susceptible women acquire HSV infection during pregnancy. Acquisition of infection with seroconversion completed before labor does not appear to affect the outcome of pregnancy, but infection acquired near the time of labor is associated with neonatal herpes and perinatal morbidity.

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