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Genital Herpes In Pregnancy-A Literature Review

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Abstract

The hospital is one of the institutions engaged in health services. The main indicator of the standard of a health facility and is a measure of the quality of service, low customer satisfaction will have an impact on the number of visits that will affect the profitability of health facilities. This study aims to determine the effect of quality and the dominant variables that affect service on patient satisfaction at the Haji-Medan Hospital in 2020. The quantitative research was conducted through an analytical survey research approach with a cross sectional study approach. Testing through logistic regression on the independent variables, namely; Reliability, Responsiveness, Assurance, Empathy and Tangible from the respondents' questionnaire data as many as 80 samples. The results showed that service quality had a significant effect on patient satisfaction from four variables, namely; reliability p value 0.020 (p < 0.05), responsiveness p value 0.038 (p < 0.05), empathy p value 0.000 (p < 0.05), p value tangible 0.001 (p < 0.05). Assurance variable, the quality of health services has no effect on patient satisfaction with a p value of 0.332 (p> 0.05). The dominant variable affecting patient satisfaction is the empathy variable. It is recommended to improve services from the aspect of assurance in order to increase patient confidence in getting services so that patients can feel satisfied with the services provided.

Introduction

HSV is a DNA virus that consists of two primary strains, namely HSV-1 and HSV-2. It is known as one of the deadly infections in pregnancy, namely TORCH-S (Toxoplasmosis, Rubella, Cytomegalovirus, Herpesvirus, Syphillis). 1 HSV-1 is often acquired during early childhood through nonsexual contact and often results in orolabial lesion, less commonly on the genitals. HSV-2 is predominantly transmitted through sexual intercourse and primarily results in genital outbreaks (Baghel & Inamdar, 2020; Wafaa Ali Belail Hammad, 2021). HSV infection is a prevalent sexually transmitted infection among women in their reproductive years, particularly HSV-2, which is acquired through sexual intercourse (Wafaa Ali Belail Hammad, 2021).

HSV infection is a persistent and recurring condition that lasts throughout a person's life. The frequency of its recurrence primarily relies on the host's immune system (Baghel & Inamdar, 2020). Pregnant women are susceptible to this due to their impaired immune system (Kumar M, Saadaoui M, 2022; Vilibic-Cavlek et al., 2024). While mostly benign, genital infections with HSV can pose a threat to the developing foetus and baby through mother-to-child transmission (MTCT) (Kumar M, Saadaoui M, 2022; Vilibic-Cavlek et al., 2024). This review

seeks to provide a detailed review of genital herpes during pregnancy, including its effects on the development of the foetus, as well as strategies for its management.

Etiology

HSV is a double-stranded DNA virus that can be classified into HSV type 1 (HSV-1) and HSV type 2 (HSV-2) based on the glycoproteins found in the lipid bilayer envelope. HSV belongs to Orthoherpesviridae family, genus Simplexvirus (Vilibic-Cavlek et al., 2024). HSV-1 is linked to glycoprotein G1, while HSV-2 is linked to glycoprotein G2. HSV-1 mainly causes orolabial disease, whereas HSV-2 causes genital manifestations of the disease, gingivostomatitis, and keratoconjunctivitis (Patton et al., 2018). Both types of herpes are extremely contagious in pregnant women and can be passed from the mother to the newborn through the bloodstream or most likely after vaginal childbirth, resulting in neonatal herpes and an elevated mortality rate (Hosseini et al., 2023).

Epidemiology

Approximately 500 million individuals worldwide have been infected with HSV. The exceptionally large number of positive cases globally can be ascribed to the extremely contagious nature of this virus (Hosseini et al., 2023). According to a 2017 report by the World Health Organization (WHO), the global prevalence of HSV-1 and HSV-2 infections among individuals under the age of 50 is 67%. The frequency of HSV-2 infection among females aged 14 to 49 has been found to be as high as 15.9% (Nath et al., 2021).

The prevalence of herpes infection during pregnancy varies across countries. In Italy, the prevalence is relatively low, specifically ranging from 7.6% to 8.4% (Hollier & Jamieson, 2020). However, a study conducted by Vora et al. in a tribal region in India found a higher prevalence of herpes infection among pregnant women screened for TORCH, with a rate of 38%. Among these cases, 4% showed IgM positivity, indicating primary infection (Vora et al., 2020). The worldwide occurrence of neonatal herpes is estimated to be 10.3 cases per 100,000 live births. However, the reported incidences per live birth differ across countries, ranging from 4.7 cases per 100,000 in the Netherlands to 71.8 cases per 100,000 in Malawi (Wafaa Ali Belail Hammad, 2021).

Pathophysiology

HSV is transmitted via direct contact with individuals who are seropositive and actively shedding the virus. The virus primarily targets the skin and mucosa, infecting epithelial cells upon initial contact and then reproducing within these tissues (Vora et al., 2020; Xu et al., 2019). Following the initial exposure and subsequent disappearance of symptoms, often within a period of 10-14 days, the virus enters a dormant state within the periaxonal sheath of sensory nerves located in the trigeminal, cervical, lumbosacral, or autonomic ganglia. During reactivation, the virus migrates along the sensory nerves to the mucocutaneous site, where it replicates and forms a cluster of vesicles at the dermatological location of the sensory neuron (Gopinath et al., 2023; Zhu & Viejo-Borbolla, 2021).

HSV-2, specifically, might manifest as an initial infection characterized by the presence of painful genital ulcers, sores, crusting, uncomfortable lymph nodes, and painful urination. The typical manifestation is a flat or raised lesion on the skin and mucous membranes that transforms into fluid-filled blisters and pus-filled lesions, often persisting for a duration of 3 weeks. Lesions typically appear on the glans penis or penile shaft in men, and on other areas such as the vulva, perineum, buttocks, vagina, or cervix in women. 11-13 Common symptoms include encompass discomfort, particularly in the vulva in females, a sensation of burning, and painful urination. Lymphadenopathy, fever, and cervicitis (in women) or proctitis (in men) are frequently observed concurrent symptoms.

Following the initial infection, the virus establishes a permanent state of inactivity in sensory nerve ganglions, particularly in the sacral ganglion (Kumar M, Saadaoui M, 2022; Mustafa et al., 2016). If there is a trigger, such as an immunogenetic predisposition, the virus has the ability to become active again and cause recurring infections. However, the likelihood of reactivation diminishes as a person becomes older. Several physiological and environmental conditions, such as fever, exposure to UV radiation, menstruation, stress, or trauma, might act as triggers. The frequency of genital HSV-2 infections might differ significantly among individuals and can even change over time within the same person. Recurrent infections induced by HSV-2 are approximately 16 times more frequent than HSV-1 genital infections, occurring on average 3-4 times each year. HSV-2 is mostly spread by individuals who have tested positive for HSV-2 antibodies, and it affects nearly everyone who has detectable levels of anti-HSV-2 IgG antibodies. 11-13 On the other hand, the occurrence of HSV-1 shedding is infrequent. These data suggest that persons who test positive for HSV-2 should always be regarded as possible carriers of the virus. Recurrence is a common phenomenon in individuals with symptomatic primary genital herpes caused by HSV-2. Recurrence caused by HSV-1 happens at a frequency that is more than five times lower.

Typically, endogenous viral reactivation is marked by the release of viruses without any noticeable symptoms. Recurrent genital herpes lesions can also occur as a result of endogenous viral reactivation. Recurrence is typically first identified by prodromal symptoms, such as neuralgia, dysaesthesia, or lumbosacral dermatomal pain, which occur 1-2 days prior to the emergence of skin and mucosal lesions. In contrast to the initial infection, symptoms during subsequent bouts are far less severe and resolve more rapidly. Typical symptoms of recurring HSV-2 infection consist of several small, grouped, fluid-filled sores in the genital region, however they can also appear in other areas around the genitals, such as the groin, buttocks, and thighs. Lesions may manifest either at the same site as the initial infection or relocate to a different area. The reappearance of genital sores can be identified by symptoms such as sensitivity, itching, stinging, or lack of sensation. Untreated, the lesions often resolve within a span of 6 to 10 days. Recurrent herpetic cervicitis is less frequent, affecting only 12% of individuals, and it might manifest without any visible exterior sores (Vora et al., 2020; Xu et al., 2019).

Classification

The genital herpes simplex virus (HSV) infection can be clinically classified into three categories: primary episode, non-primary first episode, and recurrent (Wafaa Ali Belail Hammad, 2021). A primary episode refers to the initial appearance of a genital herpetic lesion in a patient who does not have any pre-existing antibodies for either HSV-1 or 2 (De Rose et al., 2023; Riley & Wald, 2008). Nonprimary first-episode refers to a situation when a patient experiences their first occurrence of a genital HSV lesion, but they already have HSV antibodies that are different from the specific HSV type seen in the genital lesion. For instance, HSV-2 is isolated from the genital sore of a patient who already has HSV-1 antibodies but does not have HSV-2 antibodies. This is the most frequent occurrence, especially in people who have a past medical history of orolabial herpes (De Rose et al., 2023; Riley & Wald, 2008). A recurrent episode refers to a situation where a patient shows symptoms of a herpes infection, and the type of HSV found in the genital lesion is the same as the type of HSV that the patient already has antibodies for in their bloodstream (De Rose et al., 2023; Riley & Wald, 2008). In patients who previously had no symptoms of genital infection, a recurrence of symptoms may be the first instance of genital herpes that is detected. Accurate classification typically necessitates the use of both type-specific serologic and virologic assays, unless there is already well-documented evidence of recurrent HSV that has been confirmed by culture or polymerase chain reaction (PCR) (Baghel & Inamdar, 2020; Kumar M, Saadaoui M, 2022). Antibodies that

are specific to the HSV often form within the initial 12 weeks following infection and remain present indefinitely.

Precise categorization is especially crucial during pregnancy due to the fact that a recent infection genital infection (either primary or nonprimary first-episode) near the time of delivery poses a significant risk for transmission to the newborn. Whereas recurrent infection poses a lower risk of neonatal herpes (De Rose et al., 2023; Riley & Wald, 2008).

Genital Herpes In Pregnancy

Infections are a major threat to human reproductive health. Infections during pregnancy can result in premature birth or stillbirth. Additionally, these diseases can be passed to the fetus, causing congenital infection that increases morbidity and mortality of neonates (Chudnovets et al., 2020; Megli & Coyne, 2022). HSV infections exhibit comparable clinical manifestations in both pregnant and nonpregnant women, typically presenting as either asymptomatic or accompanied by mild symptoms. Orofacial disease is characterized by the presence of individual or grouped fluid-filled blisters on the face and lips. In contrast, genital HSV blisters are found on the genitalia, perineum, buttocks, upper thighs, or perianal regions. The HSV rash has the potential to develop ulcers before it eventually resolves. Constitutional symptoms such as malaise, fever, or regional adenopathy may show (Chudnovets et al., 2020).

The presentation of herpes infection in pregnant women is dependent upon the specific viral strain and the timing of the infection (De Rose et al., 2023). The clinical presentation of HSV-1 infections often tends to be mild. HSV-2 infections are a significant medical concern for women of reproductive age since the virus can be passed on to unborn babies and newborns. Primary HSV infection in pregnant women can be more severe than in non-pregnant women, when compared to recurrent HSV infection. Maternal infection can happen at any point during pregnancy. Genital HSV infections occurring during pregnancy are linked to miscarriage, impaired fetal growth, premature birth, as well as the development of herpes in newborns. Both primary and recurrent maternal infections can cause congenital disease, but the risk after recurrent infection is low. Neonatal herpes is more common (50%) in infants born to mothers with a primary HSV infection than in infants born to mothers with recurrent HSV (<3%). Specifically, acquisition of infection may affect pregnancy trimesters differently. 20.

Methods

First and Second Trimester

Congenital infection can occur during the first and second trimester by either hematogenous transmission or ascending infection with intact membranes. This method of transmission is relatively uncommon, occurring in less than 5% of first infections (Wafaa Ali Belail Hammad, 2021). The transplacental transmission of the virus is highly plausible (Baghel & Inamdar, 2020).

In pregnant women, primary HSV infection with viremia can lead to intrauterine infection. This infection is associated with placental infarction, necrotizing calcifying mycosis (inflammation of the umbilical cord), plasma cell infiltration, fetal hydrops, and potentially even fetal death. The herpesvirus primarily targets epithelial cells found in the skin and mucous membranes, as well as neurons. HSV infection can cause the loss of HLA-G by obstructing its intracellular transit in the placenta, which contributes to the pathophysiology of the infection. HSV has the ability to invade human trophoblast cells, resulting in either cell death or decreased production of human chorionic gonadotropin. HSV has the ability to suppress the production of many proinflammatory cytokines, such as IFN-α/β, TNF-α, IL-6, IL-12, and RANTES, by decreasing the durability of mRNA. Therefore, HSV has the ability to impede the host's immune response to infection. IL-12, in conjunction with several cytokines, stimulates the synthesis of IFN-γ, primarily in NK cells, to initiate the elimination of infected cells (Kumar

M, Saadaoui M, 2022; Riley & Wald, 2008). In the course of transmission, there is an increased risk abortion and premature delivery. If born, the neonate may have the characteristic triad of skin vesicles, ulcers, and scars, eye injuries, and severe abnormalities of the CNS, including microcephaly or edema (Riley & Wald, 2008).

Third Trimester

Neonatal infection is most commonly transmitted through direct contact with viral lesions in the vaginal canal during birth, a process known as vertical transmission Consequently, when a mother is infected with HSV around the time of giving birth, the chances of transmitting the disease to the baby are increased (Kumar M, Saadaoui M, 2022). Most cases of neonatal herpes infections are acquired during childbirth, with 60% to 80% of cases occurring in women who acquired HSV in the third trimester, close to the time of delivery (Baghel & Inamdar, 2020). Neonates born through the vaginal route to these women have a chance of infection ranging from 30% to 50%, whereas neonates born to mothers with recurrent HSV have a risk of infection less than 1%. Ascending infection typically arises following an extended rupture of fetal membranes in moms who have HSV infection near the active stage at the time of delivery. Occasionally, it occurs without a ruptured amniotic membrane (Riley & Wald, 2008). The difference in infection risk is believed to be due to larger levels of HSV virus after the first infection compared to a subsequent infection. Moreover, obtaining HSV in the short term does not provide enough time for the development of antibodies that can pass through the placenta and offer protection to the newborn for a period of 6 to 12 weeks. The likelihood of vertical transmission is roughly 25% during an initial-nonprimary episode, which is due to the partial protection provided by antibodies against the other virus serotype. In newborns infected at or after birth, herpesvirus infections can appear as localized skin, eye, and/or mouth disease, HSV encephalitis, or disseminated HSV infection. Disseminated HSV infection can cause severe dysfunction in several organs and has a mortality rate of over 80% in untreated patients. Out of the neonates that are affected, 50% have infections that are limited to a specific area, 33% have infections that involve the central nervous system (CNS), and 17% have infections that have spread throughout the body (Vilibic-Cavlek et al., 2024).

Result and Discussion

Diagnosis

It is necessary for all women who are believed to have genital herpes infection to undergo laboratory examination. Confirmation of infection can be achieved by two methods: viral detection and antibody detection. Patients who have vaginal vesicles, ulcers, or other mucocutaneous lesions should undergo virologic tests, which involve viral culture and HSV antigen detection using polymerase chain reaction (PCR). 18-20 Patients with a clinical history indicating HSV, but without visible sores or with negative culture or PCR test findings for lesions, may benefit from type-specific serologic assays. These assays accurately differentiate between HSV-1 and HSV-2 antibodies. The antibody detection approaches encompass the utilization of laboratory-based and point-of-care serologic tests to identify the existence of antibodies to HSV-1 or HSV-2. Antibodies against HSV are produced throughout the initial weeks following infection and are present indefinitely. Hence, if there is a strong clinical suspicion of herpes and a recent infection is suspected, it may be necessary to conduct additional serologic tests (Patton et al., 2018). The diagnosis of herpes infection during pregnancy might be challenging because it often does not cause any symptoms. Nevertheless, the American College of Obstetrics and Gynecology (ACOG) advises against regularly testing for HSV serostatus during pregnancy due to insufficient evidence supporting its cost-effectiveness (Patton et al., 2018). Pregnant women should undergo screening for a previous occurrence of genital herpes. There is currently no new information that supports the need for regular testing of pregnant women for serologic evidence of HSV infection.

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Treatment

Genital herpes infection are managed using antivirals. The regimen of therapy is dependent upon the timing of HSV acquisition. For primary HSV, antiviral treatment should be administered orally to pregnant women to reduce the duration and the severity of the symptoms as well as reduce the duration of viral shedding (Patton et al., 2018). Antiviral treatment for HSV is used not only to relieve symptoms in pregnant women, but also as a preventive measure during the late third trimester until labor begins. The goals of prophylaxis are to decrease the risk of active HSV disease at the time of delivery and to reduce asymptomatic viral shedding, thus minimizing maternal morbidity and peripartum MTCT (Rogan & Beigi, 2019). This is given as a suppressive therapy. The goals are to diminish the likelihood of active HSV disease during delivery and to minimize asymptomatic viral shedding, thereby reducing maternal morbidity and the transmission of the virus to the newborn during childbirth (Rogan & Beigi, 2019).

For primary HSV and non-primary first-episode HSV, suppression from 36 weeks of gestation should be commenced. Regarding the mode of birth, providing that labour and/or birth does not ensue within the next 6 weeks, the pregnancy should be managed expectantly and vaginal birth (at viability) anticipated. For women experiencing many recurrent lesions, a suppressive treatment should be initiated starting from 36 weeks of pregnancy and continued until childbirth. Mode of delivery should be vaginal unless there are additional medical reasons for a cesarean section.If diagnosis is made in the third trimester, it should be treated in the same as a 'first episode', followed by suppressive treatment. For women who experience their first episode of genital herpes in the third trimester of pregnancy, especially if symptoms appear within 6 weeks of the expected birth, it is advisable to opt for caesarean section as the preferred mode of delivery. The likelihood of neonatal transmission of HSV is exceedingly high. IF spontaneous rupture of the membranes occurs, caesarean section should be performed as soon as possible, preferably within 4 hours.

An analysis of randomized clinical trials found that starting suppressive treatment with acyclovir at 36 weeks of gestation resulted in a 75% reduction in clinical recurrence of HSV at delivery, a 70% decrease in caesarean deliveries due to recurrent genital HSV, and a 91% and 89% decrease in the risk of HSV viral shedding and total HSV detection at delivery, respectively. A comparable meta-analysis, which incorporated valacyclovir, reported similar findings. 28

Table 1. Antiviral therapy for herpes infection in pregnancy 6,29,32

Indication	Acyclovir	Valacyclovir
Primary infection	400 mg per oral, three times daily, 7-10 days	1 g per oral, twice daily, 7-10 days
Symptomatic recurrent infection	400 mg per oral, three times daily, 5 days ***or*** 800 mg per oral, twice daily, 5 days	500 mg per oral, twice daily, 3 days ***or*** 1 g per oral, once daily, 5 days
Suppression therapy	400 mg per oral, three times daily, from 36 weeks gestational age until delivery	500 mg per oral, twice daily, from 36 weeks gestational age until delivery
Severe / disseminated disease BW = *body weight*	5-10 mg/kgBW intravenous, every 8 hours, for 2-7 days and continued with oral therapy for primary infection to complete 10 days of therapy	

Neonatal Outcomes Of Hsv Infection

Neonatal herpes is defined as the diagnosis of an HSV infection in a neonate within the first 28 days of life. Infection with either HSV-1 or HSV-2 during pregnancy can happen at any point, and the outcome of neonatal herpes infection depends on factors such as the trimester of infection and whether it is a first-time or recurring infection in the vaginal area. Neonatal HSV can be classified into three primary categories: localized infections affecting the skin, eyes, and oral cavity (SEM); infections involving the central nervous system (CNS), with or without SEM; and transmitted disease. 19 Untreated cases of neonatal herpes infection can lead to a mortality rate ranging from 50% to 80% 2.

HSV infection localized to the skin, eyes, and mucosal regions constitutes 45% of newborn infections. If this condition is promptly recognized, newborns usually respond favorably to intravenous acyclovir, which prevents the spread of the infection throughout the body and leads to positive clinical results. 30 CNS infections constitute 30% of all infections and provide challenges in diagnosis due to their nonspecific symptoms, such as lethargy, poor feeding, seizures, and the potential absence of lesions. Treatment reduces the mortality rate from 50% to 6%. Nevertheless, most newborns will still need ongoing monitoring to ensure they reach their neurodevelopmental milestones, as well as regular tests of their vision and hearing. Disseminated Herpes Simplex Virus (HSV) constitutes a quarter (25%) of all infections and has the potential to lead to failure of several organs. Despite receiving therapy, there is a 31% chance of death associated with this condition. 24 Hence, the primary objective in controlling HSV infection during pregnancy is to concentrate therapeutic efforts on preventing transmission to the newborn. 31.

Conclusion

HSV infection is prevalent among pregnant women. The fetal consequences of HSV infection, particularly HSV-2, are highly substantial. This emphasizes the significance of recognizing and treating the illness based on the time of the infection. Maintaining a high index of suspicion,, promptly diagnosing, and promptly treating during acute and recurring episodes will decrease the likelihood of vertical transmission and subsequent neonatal complications.

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