Original Article

The Prevalence of Herpes Simplex Virus 1, 2 Infections in Blood Donating Volunteers and the Association with Demographic Parameters

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Abstract

Background: HSV-1 and 2 refer to two types of herpes simplex virus. HSV-1 is associated with oral herpes whereas HSV-2 is linked to genital herpes. **Objectives:** The aim of the current study was to determine the prevalence of recent and past HSV-1 + 2 infections in a randomly selected group of volunteers and to find the possible association between the viral infection and the study parameters. **Materials and Methods:** This is a cross-sectional study conducted in the period from November 2022 to February 2023, involved 250 blood donor volunteers who attended to Duhok Blood Bank. The samples were then transferred to Shekhan Technical Health College, Medical Laboratory Department, where they were tested by HSV-1, HSV-2 IgG/IgM Antibody Rapid Test Cassette. **Results:** The mean age was 37.38 ± 0.561 (± SE) with a range of 19–77 years. Very few cases showed a positive reaction to anti-HSV 1 + 2 IgM antibodies thus they were omitted from the final analysis. It is shown that 82% were anti-HSV 1 + 2 IgG positive whereas only 18% were negative. The lips represented the most affected part (53.2%). The middle age groups were the highly infected ones. Gender difference showed no association with anti-IgG positivity while the residence of the participants, the marital status, and the formation of blisters were all statistically significantly associated with anti-IgG positivity ($P = 0.045$, $P = 0.004$, $P \leq 0.001$, respectively). The facial distribution of the blisters was statistically significantly associated with the IgG status ($P \leq 0.001$). Finally, no association has been found between several interferences with the anti-HSV IgG status. **Conclusion:** HSV continued to show higher infectivity and spread. The virus expresses different affinities for infection sites and results in a nearly characteristic infectious lesion. Multiple study parameters appeared to be unevenly associated with the virus infection.

Keywords: Blisters, genital herpes, herpes simplex virus, HSV-1, HSV-2 IgG/IgM Antibody Rapid Test Cassette, oral herpes

Introduction

Herpes simplex virus (HSV) is a highly transmissible virus that can lead to infections in humans. It belongs to the family of Herpesviridae and is classified into two types: HSV-1 and HSV-2. HSV-1 is responsible for oral herpes, which may cause by cold sores or fever blisters, whereas HSV-2 is responsible for genital herpes (wherever HSV is mentioned, it indicates both types 1 and 2 unless a specification is pointed out). Both types of herpes are lifelong infections that can cause recurrent outbreaks of painful blisters and ulcers.[1,2]

HSV infections are widespread affecting an estimated 491 million individuals globally. The virus is spread by close contact with an infected subject or by coming into contact with infected saliva and body fluids, genital secretions, or herpes lesions. Herpes infection can also be transmitted from an infected mother to her newborn during childbirth, which can be life-threatening to the baby. HSV-1 is more prevalent than HSV-2, with up to 90% of the global population infected with HSV-1 by the age of 50. However, HSV-2 is more common in some areas of the world, particularly in sub-Saharan Africa, where up to 80% of adults may be infected. The prevalence of

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HSV-2 varies widely across populations and is generally greater among females than males. The prevalence of HSV-2 also rises with age, with the highest rates detected in people between 40 and 49 years.[1,3]

While there is no treatment for herpes, antiviral preparations can aid manage the symptoms and reduce the frequency of outbreaks. In addition, practicing safe sex and avoiding close contact with people who have active herpes lesions can help prevent the spread of the virus. The diagnosis of herpes simplex virus (HSV) is based on clinical symptoms and laboratory tests. A viral culture or polymerase chain reaction (PCR) test can prove the existence of the virus in a sample taken from a lesion. Blood tests can also detect HSV antibodies, which can indicate a recent or past infection. Serologic tests are less precise than viral culture or PCR tests for diagnosing active HSV infections but may be helpful for screening for former infections.[4,5]

Research on HSV continues to advance, with new treatments and vaccines being developed. Understanding the virus and its modes of transmission is important for both preventing and treating herpes infections.[6,7]

The aims of the current study were to determine the prevalence of recent and past HSV-1 + 2 infections in a randomly selected group of volunteers and to find the possible association between the viral infection and the study parameters.

Materials and Methods

This cross-section study was carried out at Duhok Polytechnic University, Shekhan Technical Health College, Department of Medical Laboratory Technology, Kurdistan Region, Iraq, during the period from November 2022 to February 2023 to assess the seroprevalence of HSV type-l and type-2 antibodies in healthy blood donors. The samples were 250 blood donors at Duhok Blood Bank; their ages ranged between 19 and 77 years, 199 were males, and 51 were females. The volunteers were supplemented with questionnaires including the following parameters: Name, age, gender, residence area, marital status, history of blisters, site of infection, occupation, and whether the participant had practiced blood transfusion, surgery, tattooing, and tooth extraction. The blood samples were collected from the donors in serum separation tubes, tubes were allowed to stand for half an hour then centrifuged for 20 min at 3000 rpm, sera were then recovered in Eppendorf tubes and stored at -20 for later use. The following diagnostic kits were used throughout the present study, HSV-1, HSV-2 IgG/IgM Antibody Rapid Test Cassette manufactured by Biozek Medical (Netherlands).

Assay procedure

Primarily, samples were brought at room temperature to thawing for 30 min; cassettes were treated the same way as well. Next, one drop of serum with two drops of the buffer was added to each cassette, and the results were observed after 15–20 min. Results were interpreted as positive or negative, if appeared after 20 min considered invalid.

Statistical analysis

The statistical analysis of data was carried out using SPSS (IBM Corporation, New York, NY, USA) (version 28.0) software. Data was presented by count and proportion if categorical, by mean ± SE if numerical, Chi-square of independence test was used to determine the presence of a statistically significant association. $P \leq 0.05$ was considered statistically significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to document number 110122022-3 on December 14, 2022.

Results

Table 1 shows the demographic data of the participants, it appears that the middle age groups assumed the higher

Table 1: Demographic data of the participants

Sex	Marital status	Residency								Total
		Urban				Rural				
		Age categories (years)				Age categories (years)				
		15–25	26–35	36–45	>46	15–25	26–35	36–45	>46	
		Count	Count	Count	Count	Count	Count	Count	Count	
Male	Married	3	31	42	17	3	21	28	21	166
	Non-married	12	11	2	0	4	3	1	0	33
Female	Married	0	7	19	3	0	2	7	0	38
	Non-married	0	8	0	0	1	4	0	0	13
	Total	15	57	63	20	8	30	36	21	250

count of all parameters. The mean age of the subjects ± SE was 37.38 ± 0.561, the minimum age for a participant was 19 years and the maximum was 77 years. The study involved 199 (79.6%) males and 51 (20.4%) females.

It is shown that when the participants were classified according to their job description, 41.6% were free workers and government employees as well while those who were jobless constituted 16.8 of all subjects. Furthermore, 18% of the subjects tested negative for anti-HSV-1 + 2 IgG while 82% showed positive serum reaction. It is also revealed that 64.4% of all cases had a blood transfusion, 15.2% practiced different surgeries, 6.8% tattooed their bodies, and 13.6% had tooth extraction experiments. Finally, the majority of the candidates (82. 8%) showed blisters in different places on their faces while the rest 17.2% have not revealed such facial manifestations [Figure 1a–d], respectively.

The physical examination of the candidates revealed the distinct distribution of facial lesions (blisters), obviously, the lips were the main affected site and constituted nearly half (50.2%) of the lesions that appeared on the face while the tongue was the least affected organ (4.0%) [Figure 2].

Table 2 shows the association of age categorization with the past infection status of the HSV 1 + 2, it shows fairly clear, despite without statistical significance (χ^2 [3, n = 250] = 6.143; P = 0.991), that the higher percentages of affected age categories were those in the middle age period represented by 80.5% and 86.9% for the 26–35 years and 36–45 years, respectively.

A Chi-square test was performed for a group association between HSV IgG status and gender, residency, marital status, and whether blisters appeared or not, no statistically significant association was observed when gender was considered (P = 0.088) while statistically significant associations were found when the rest three factors were taken into consideration (P = 0.045, P = 0.004, P < 0.001, respectively) [Table 3].

The results of this study revealed that the facial lesions of HSV infection are not uniformly distributed, the lips being the most severely affected area with a frequency of 125 out of a total of 250 victims while the tongue was the least infected organ that appeared in 10 subjects out of the 250 participants. The association of the facial blister site with the HSV infection status was very highly statistically significant

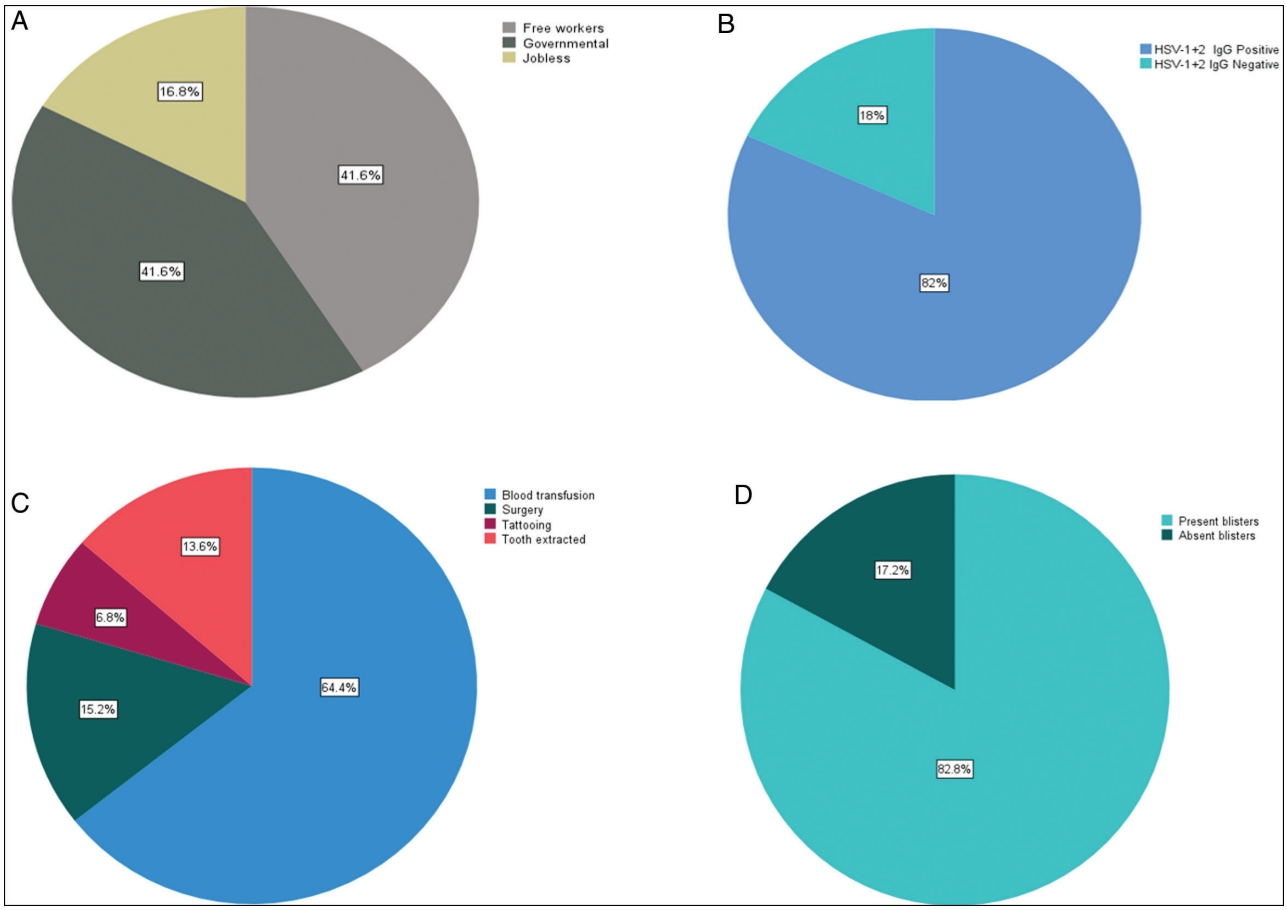

Figure 1: General description of the output. (a) Job descriptions of the participants, were categorized into three categories. (b) The serum IgG test results (positive and negative). (c) Previous exposures to different kinds of interventions. (d) Description of whether each individual had experienced the presence of facial lesions (blisters)

with a large effect size indicated by Cramer's V value (χ^2 [4, n = 250] = 137.517, P < 0.001, Cramer's V = 0.742) [Table 4].

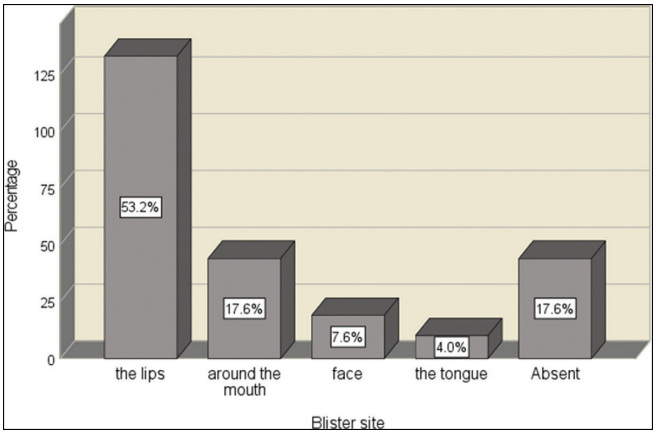

Figure 2: Facial manifestations represented by the blister sites and the relevant percentage of each type of lesions

The risk of HSV infection from blood transfusion, surgery, tattooing, and tooth extraction is generally low, an observation that has been confirmed in the present work, despite the higher count of some cases of interference (blood transfusion) that seemed linked to the positivity of the past infection, but the finding was statistically insignificant (χ^2 [3, n = 250] = 3.36, P = 0.339) [Table 5].

Discussion

HSV-1 and HSV-2 are the most common herpes viruses that infect humans, and they can cause oral or genital herpes. Oral herpes is typically caused by HSV-1, and it can cause cold sores or fever blisters on or around the mouth. Genital herpes, which is typically caused by HSV-2, can cause painful sores or blisters on or around the genitals.[8] Although this pathogenic virus was discovered more than 2000 years ago, it recently infected many people, and many more have died due to this pathogen.[9] In 2016, more than

Table 2: The rate of infection distributed according to age groups

HSV IgG	Count and %	Age (years)					
		15–25	26–35	36–45	>46	Total	*P* value
Positive	Count	15	70	86	34	205	0.991
	Percentage, %	65.2	80.5	86.9	82.9	82.0	
Negative	Count	8	17	13	7	45	
	Percentage, %	34.8	19.5	13.1	17.1	18.0	
Total		23	87	99	41	250	
		100.0%	100.0%	100.0%	100.0%	100.0%	

Table 3: The association between the infection status and gender, residency, marital status, and blister formation

Factor	Level	HSV IgG positive count (%)	HSV IgG negative count (%)	Total (%)	*P* value
Gender	Male	159 (79.9)	40 (20.1)	199 (100)	0.088
	Female	46 (90.2)	5 (9.8)	51 (100)	
Residency	Urban	133 (85.5)	22 (14.2)	155 (100)	0.045*
	Rural	72 (75.8)	23 (24.2)	95 (100)	
Marital status	Married	174 (85.3)	30 (14.7)	204 (100)	0.004**
	Non-married	31 (67.4)	15 (32.6)	46 (100)	
Blisters	Present	197 (95.2)	10 (4.8)	207 (100)	<0.001***
	Absent	8 (18.6)	35 (81.4)	43 (100)	

*Significant at P < 0.05.

**Significant at P < 0.01.

***Significant at P < 0.001

Table 4: The distribution of facial lesion in relation to HSV infection status

HSV IgG	Count and %	Blister site						
		The lips	Around the mouth	The face	The tongue	Absent	Total	*P* value
Positive	Count	125	43	18	10	9	205	<0.001***
	Percentage, %	94.0	97.7	94.7	100.0	20.5	82.0	
Negative	Count	8	1	1	0	35	45	
	Percentage, %	6.0	2.3	5.3	0.0	79.5	18.0	
Total		133	44	19	10	44	250	
		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

***Significant at P < 0.001

Table 5: The association of some medical interferences with the infection status

HSV IgG		Interference					
	Count and %	Blood transfusion	Surgery	Tattooing	Tooth extraction	Total	*P* value
Positive	Count	130	34	12	29	205	0.339
	Percentage, %	80.7	89.5	70.6	85.3	82.0	
Negative	Count	31	4	5	5	45	
	Percentage, %	19.3	10.5	29.4	14.7	18.0	
Total		161	38	17	34	250	
		100.0%	100.0%	100.0%	100.0%	100.0%	

13% of the world's people between the ages of 15 and 49, or about 491 million people, were thought to be living with a HSV-2 disease.[10]

Serological diagnosis of HSV 1 and 2 can have a significant impact on patient care and management. Serological testing can be particularly useful in cases where clinical symptoms are unclear or absent, or in cases where patients may not have sought medical attention during their initial outbreak. Serological testing can also help differentiate between HSV-1 and HSV-2 infections, which can have different clinical presentations and treatment strategies. However, it is important to note that serological testing has limitations, including the potential for false positive or false negative results. Therefore, clinical correlation and appropriate counseling are important in interpreting serological results. The current study relied mainly on the serological testing of IgM and IgG to confirm early and late infections, respectively. The results indicated a very low early infection rate thus they were omitted from the final output.[11,12]

The prevalence of HSV IgG antibodies is generally higher than that of IgM antibodies because IgG antibodies persist for a longer time after infection, while IgM antibodies tend to decline more rapidly. This statement supports what the results of this study came up with regarding the very low number of cases that reported positive anti-HSV IgM antibodies. Moreover, according to a study published in the Journal of Clinical Microbiology, IgG antibodies against HSV-1 and HSV-2 can persist for a lifetime, while IgM antibodies tend to decline within a few months after infection.[13] Another study published in the Journal of Infectious Diseases found that the sensitivity and specificity of IgM tests for detecting HSV infections were lower than those of IgG tests and that IgM tests had a higher rate of false positive results.[14] The authors concluded that IgG tests were more reliable for diagnosing both primary and recurrent HSV infections. Overall, while both HSV IgG and IgM tests can be useful in diagnosing HSV infections, IgG tests are generally preferred due to their higher sensitivity, specificity, and persistence over time. Gender and age are important factors that influence the epidemiology of HSV infection. The results of this work were contrary to those reported by another study[15] that has shown HSV-1 is more common than HSV-2 and that both types of HSV are more prevalent among women than men. However, the prevalence of HSV-1 infection increases with age and is highest among individuals over 50 years of age, while the prevalence of HSV-2 infection is highest among people aged 20–29 years; the later findings were generally consistent with the results of the current study. Interestingly, both males and females can be affected by HSV-1 and HSV-2 infections, and the prevalence of these viruses is similar among both genders. However, some studies suggest that men may be more likely to acquire genital herpes due to their greater likelihood of engaging in high-risk sexual behavior, such as having multiple sexual partners or engaging in unprotected sex.[3,16] On the other hand, the results of this work were inconsistent with two other studies conducted in the United States and Netherlands, both reported higher infection rates in females compared to males with HSV-1, 2.[17,18] In terms of clinical manifestations, females are more likely to experience severe and recurrent outbreaks of genital herpes than males. This may be due to hormonal factors, as outbreaks tend to occur more frequently during menstruation or pregnancy.[19]

Age is also an important factor in HSV infection, overall, the results of this study agreed with what was stated before that the prevalence of HSV-1 increases with age due to greater exposure to the virus over time. The prevalence of HSV-2 is highest among middle-aged people, which may be related to high rates of sexual activity during this age period.[20]

HSV is a common viral infection that can cause facial lesions. The differential expression of these lesions can vary depending on the type of HSV virus, the stage of the infection, and the location of the lesion. Typically, the lesions appear as clusters of small, fluid-filled blisters that can be painful and itchy. In some cases, the blisters may merge to form a larger, open sore or ulcer. Additionally, the lesions may appear on different areas of the face, such as the lips, cheeks, or nose. The severity and duration of the lesions can also vary depending on individual factors such as the person's immune system and overall health.[21,22] Within the facial region, HSV infection can cause lesions in different locations with varying frequency. The results of the present investigation came in

line with two studies, first where the most common location for facial HSV-1 lesions was the lips (96%), followed by the nose (8%) and cheek (2%); second with a study f that found 54% of HSV-1 facial lesions occurred on the lips, while 22% occurred in the nasal area, and 13% occurred in the perioral area. The latter two studies also emphasized that HSV-1 lesions on the eyelids, ears, and scalp are relatively rare but can occur.[23] The differential distribution of facial lesions in HSV infection may be related to the sites of viral entry and replication in the body. The lips and nose are common sites of viral entry, whereas the perioral area may be a site of viral replication due to the presence of hair follicles and sweat glands. The differential distribution may also be influenced by host immune responses, which can affect the course and location of HSV infection.[24]

The results of the present investigation were mostly consistent with the general notion of a low or insignificant association between various surgical interferences, blood transfusion, tattooing, and dentistry practices from one side and the infection with HSV virus from the other side.[25-29] Many recent improvements have been made to the diagnostic procedures for HSV infections. These improvements include novel viral identification approaches and serological assays. The clinical diagnosis of genital herpes would generally be validated by analytical testing, including serotyping since the serotype impacts the prognosis and the counseling. Serological testing can also be beneficial in asymptomatic people to detect whether or not they have had an infection in the past or now.[30] Current studies have identified some emerging trends in HSV epidemiology, including changes in the prevalence of the virus, the age of onset, and the distribution of HSV types. According to a recent study published in the Journal of the American Medical Association (JAMA), the prevalence of genital HSV-1 infection has increased over time, particularly in women.[31] However, another research paper published in the Journal of Infectious Diseases, indicated that the prevalence of HSV-1 infection has decreased in recent years, while the prevalence of HSV-2 infection has remained stable.[32] This trend may be due to changes in sexual behavior or increased use of antiviral medications. Furthermore, a separate investigation found that the age of onset of HSV-1 infection has shifted from childhood to adolescence and young adulthood.[33] This trend may be due to changes in social behavior or increased exposure to the virus. Finally, the prevention of HSV transmission remains a major public health priority. Consistent and correct use of physical prevention strategies can reduce the risk of transmission. In addition, daily use of oral antiviral medications can minimize the frequency of recurrences and asymptomatic shedding, and thereby reduce the risk of transmission.[34-37]

Conclusion

HSV continued to show higher infectivity and spread. The virus expresses different affinities for infection sites and results in a nearly characteristic infectious lesion. Multiple study parameters appeared to be unevenly associated with the virus infection. with several showing positive associations and others are not affected by the presence or the absence of a virus at all.

Note: Wherever HSV was mentioned, it indicated both types 1 and 2 unless a specification was pointed out.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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