

Seroprevalence of herpes simplex virus types 1 and 2 in Indian and Filipino migrant populations in Qatar: a cross-sectional survey

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Background: The epidemiology of herpes simplex virus infections is of growing interest but information on its seroprevalence in many countries is scarce.

Aims: This study aimed to measure the seroprevalence of herpes simplex virus type 1 and type 2 in Filipino and Indian men living in Qatar.

Methods: Blood serum specimens were collected from male blood donors aged ≥ 18 years in Qatar from 2013 to 2016. HerpeSelect[®] 1/2 and Euroline-WB assays were used to measure antibodies to herpes simplex virus types 1 and 2 in 120 Filipino and 325 Indian men.

Results: The seroprevalence of herpes simplex virus-1 was 84.9% (95% confidence interval (CI): 78.4–90.0%) in Filipino men and 48.3% (95% CI: 43.6–53.0%) in Indian men. The seroprevalence of herpes simplex virus-2 was 8.3% (95% CI: 4.6–13.7%) in Filipinos and 3.7% (95% CI: 2.2–5.9%) in Indians. The seroprevalence of herpes simplex virus types 1 and 2 increased with age, but this trend was only statistically significant in Indian men ($P = 0.013$ and $P = 0.011$ respectively).

Conclusions: The seroprevalence rates of herpes simplex virus-2 in Filipino and Indian men living in Qatar were similar to those found in the Philippines and India. However, the seroprevalence of herpes simplex virus-1 in Indians, while similar to that found in India, was substantially lower than that of other countries in Asia and developing countries worldwide, which needs further investigation.

Keywords: herpes virus 1, herpes virus 2, herpes simplex, seroprevalence, seroepidemiological studies, Philippines, India, Qatar

Citation: Nasrallah GK; Dargham SR; Harfouche M; Abu-Raddad LJ. Seroprevalence of herpes simplex virus types 1 and 2 in Indian and Filipino migrant populations in Qatar: a cross-sectional survey. East Mediterr Health J. 2019;25(x):xxx–xxx. <https://doi.org/10.26719/emhj.19.101>

Received: 23/04/18; accepted: 18/09/18

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Introduction

Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) are widespread lifelong infections (1–4), and are associated with mild to severe health consequences. Symptoms of HSV-1 infection include oral and facial lesions and the infection can affect the central nervous system, leading to oral, ocular, cutaneous and neural clinical manifestations such as herpes labialis (cold sores), herpetic whitlow, gingivostomatitis, neonatal herpes, blindness, meningitis and encephalitis (5,6). HSV-2 infection is one of the leading causes, if not the leading cause, of genital herpes and genital ulcer disease worldwide (3,4,7,8).

HSV-1 is generally acquired through the oral route during childhood with mild to serious morbidity, but evidence from the United States of America (USA) and Western Europe indicates a growing sexual acquisition through oral sex (5,9,10). HSV-2 is nearly always acquired sexually and is strongly associated with HIV infection (11–13), with its prevalence patterns providing key inferences about the structure of sexual networks (14). Evidence suggests also an association between HSV-1 and HSV-2 infections (15,16).

The epidemiology of HSV infections is of growing interest – the World Health Organization is leading the development of a business case for HSV vaccines to tackle this infection and disease burden (17). This effort, however, is challenged by the limited information on the current antibody prevalence (that is, seroprevalence) as well as inadequate knowledge of the epidemiology of both HSV infections in many countries (17).

We recently provided measures of HSV-1 seroprevalence (18) and HSV-2 seroprevalence (19) in 10 national Middle Eastern and North African populations currently living in Qatar, including Qatari citizens. One of the findings was an unexpectedly low seroprevalence of HSV-1 in Pakistanis, suggesting that HSV-1 seroprevalence in populations from the Indian subcontinent could be lower than global levels; the reasons for this low seroprevalence are still not known. Existing data on HSV-1 seroprevalence in Indian populations seem to support this conjecture (20–22).

Against this background, and with the availability of blood donor serum specimens from the Indian migrant population in Qatar, where Indian expatriates constitute nearly 25% of Qatar's current resident population (23), we aimed to measure the seroprevalence of HSV-1 and HSV-2 in an Indian population and compare them to other migrant populations in Qatar and Indians in

India. In addition, as data on HSV-1 seroprevalence in Filipino populations are lacking (21) and Filipino people are the third largest group of migrants in Qatar (23), we aimed to measure HSV-1 seroprevalence in a Filipino migrant population using the blood donor serum specimens available. Stressing the importance of migrant health, the limitations in global HSV-2 seroprevalence data (3,4) and the availability of serum specimens, we further aimed to measure HSV-2 seroprevalence in these two populations. Lastly, we aimed to generate inferences about the similarities and differences in the seroprevalence of HSV-1 and HSV-2 in different countries and populations in order to deepen our understanding of the global epidemiology of these two infections.

Methods

Study samples

The study samples consisted of Filipino and Indian male blood donors who donated blood between June 2013 and June 2016 at Hamad Medical Corporation, the largest provider of health care in Qatar. The blood specimens were collected – originally for other studies (24–27) – from 120 Filipino and 620 Indian male adults aged ≥ 18 years.

We stratified the Filipino sample into three age groups: ≤ 34 , 35–44 and ≥ 45 years. However, we categorized the larger Indian sample into seven 5-year age groups: ≤ 24 , 25–29, 30–34, 35–39, 40–44, 45–49 and ≥ 50 years. We chose these age groups to optimize the assessment of the age-specific seroprevalence of HSV-1 and HSV-2, given the number of specimens available for each nationality.

For the Filipino sample, we tested all 120 specimens. For the Indian sample, we used a sample size of 50 specimens per age group for the analysis. This number was calculated based on a significance level of 5% and an HSV-1 seroprevalence for each age group of 88% with a 10% precision level, and an HSV-2 seroprevalence for each age group of 2% with a 4% precision level. We based the two seroprevalence figures used for the sample size calculations on previous studies conducted in different national populations living in Qatar (18,19), as well as global data (3,4,12,21). However, as there are limited to no data on HSV types 1 and 2 in Filipino and Indian populations, we set a higher precision level. We finally used 325 specimens for HSV serology testing for the Indian sample. For each of the age groups of 25–29, 30–34, 35–39, 40–44, and 45–49 years, we randomly selected 50 specimens from the available specimens using a random number generator. For the remaining age groups (≤ 24 and ≥ 50 years), we tested all available specimens ($n = 40$ and $n = 35$, respectively).

Specimen testing

Laboratory analysis methods have been described previously (18,19,28,29). Briefly, for HSV-1 serology testing, we used the HerpeSelect[®] 1 enzyme linked immunosorbent assay (ELISA) kit (Cat. No. EL0910G-5, Focus Diagnostics, USA). In light of known limitations of false positives for HSV-2 antibody in ELISA tests, we used a two-test algorithm to identify specimens positive for HSV-2 based on previous work (19). We first used the HerpeSelect[®] 2 ELISA kit (Cat. No. EL0910G-5, Focus Diagnostics, USA) to screen the sera. We then used the Euroline-WB assay (Cat. No. DY 2531-2401-1 G, Euroimmun Laboratory, Germany) to test all the positive and equivocal sera to confirm positivity. We followed manufacturers' instructions for interpretation of each assay.

Statistical analysis

We estimated the overall and age-specific seroprevalence of HSV-1 and HSV-2 and 95% confidence intervals (CI). We examined trends in seroprevalence by age using the Cochran–Armitage test. We set the significance level at 5% and used SPSS, version 24 for all analyses.

Ethical considerations

The ethic boards of Hamad Medical Corporation, Qatar University and Weill Cornell Medicine-Qatar approved the use of the anonymized specimens.

Results

Filipino sample

The median age of the Filipino sample was 37 years. Of the 120 serum specimens tested for antibodies to HSV-1 and HSV-2, 101 sera tested positive for HSV-1, 18 sera tested negative and one was equivocal, giving an HSV-1 seroprevalence of 84.9% (95% CI: 78.4–90.0%). HSV-1 seroprevalence increased with age, from 84.6% (95% CI: 74.0–92.1%) in those aged ≤ 34 years to 88.9% (95% CI: 73.7–96.9%) in those aged ≥ 45 years, but this trend was not statistically significant (*P*-value for trend = 0.693; Figure 1A).

HSV-2 testing using HerpeSelect[®] 2 ELISA identified 10 sera as positive, 109 as negative and one as equivocal. Confirmatory testing was done on 11 specimens, and 10 were confirmed as positive and one as negative, giving an HSV-2 seroprevalence of 8.3% (95% CI: 4.6–13.7%). HSV-2 seroprevalence increased with age, from 5.8% (95% CI: 1.6–14.2%) in those aged ≤ 34 years to 10.7% (95% CI: 3.0–25.4%) in those aged ≥ 45 years, but this trend was not statistically significant (*P*-value for trend = 0.406; Figure 1B).

Indian sample

The median age of the Indian sample was also 37 years. Of the 325 serum specimens tested for HSV-1 and HSV-2 antibodies, 156 sera were positive for HSV-1, 167 were negative and two were equivocal, giving an HSV-1 seroprevalence of 48.3% (95% CI: 43.6–53.0%). HSV-1 seroprevalence increased with age, from 40.0% (95% CI: 26.9–54.2%) in those aged ≤ 24 years to 62.9% (95% CI: 47.6–76.4%) in those aged ≥ 50 years, a statistically significant trend (P -value for trend = 0.013; Figure 2A).

HSV-2 testing using HerpeSelect[®] 2 ELISA identified 20 sera as positive and 305 as negative. Confirmatory testing was done on 20 specimens, and 12 were confirmed as positive, seven as negative and one as equivocal, giving an HSV-2 seroprevalence of 3.7% (95% CI: 2.2–5.9%). HSV-2 seroprevalence increased with age, from 0.0% (95% CI: 0.0–7.2%) in those aged ≤ 24 years to 8.6% (95% CI: 2.4–20.7%) in those aged ≥ 50 years, a statistically significant trend (P -value for trend = 0.011; Figure 2B).

Discussion

Against a background of limited global data and using quality assays, we estimated the overall and age-specific seroprevalence of HSV-1 and HSV-2 in Filipino and Indian male migrant populations in Qatar. Of the Filipino sample, 85% were HSV-1 seropositive and $< 10\%$ were HSV-2 seropositive. Of the Indian sample, only 48% were HSV-1 seropositive and $< 10\%$ were HSV-2 seropositive. The seroprevalence of HSV-1 and HSV-2 in both samples showed increasing trend with age which reflects the higher cumulative exposure risk with age, as expected based on global data (3). However, this trend was not statistically significant for Filipino men.

To the best of our knowledge, this is the first time that HSV-1 seroprevalence has been reported in the literature for a Filipino population. HSV-1 seroprevalence in Filipinos was similar to that in other resident populations in Qatar (18) and to Asian populations in general (21). Of note, HSV-1 seroprevalence in Indians was much lower than that in other resident populations in Qatar (48% versus $> 80\%$) (18), and in developing countries globally ($> 80\%$) (3,21,30–32). However, it was similar to that reported in other studies on Indians, which was about 50% (20–22), which represents the home country rather than current residence, which can be explained because they had only recently migrated to Qatar.

Our findings highlight an apparent unexplained anomaly in global HSV-1 seroprevalence data: low seroprevalence in the Indian subcontinent compared with what is expected for developing countries (3,18,21,30–32). These findings also suggest that about 50% of Indians may start their sexual activity lacking protective antibodies against HSV-1, and are thus potentially at risk of genital acquisition of HSV-1, which could lead to genital herpes.

HSV-2 seroprevalence in both our Filipino and Indian samples was consistent with that found in the Philippines (33) and in India (34–37), and comparable to that found in other resident populations in Qatar (19) as well as in Asia in general (3,4). This finding probably suggests lower levels of sexual risk behaviour (14,38,39), reflecting more conservative attitudes towards sexuality in these areas.

Our study has some limitations. The sample consisted of male blood donors and is not necessarily representative of women nor of the Filipino or Indian population at large, in each country. Blood donors are a healthy population with possibly lower levels of HSV infections. Only a few sociodemographic attributes were gathered, limiting the potential to assess associations with infection status. Although we used high-quality and validated commercial assays, existing data suggest potential population variation in assay sensitivity and specificity (40), which may affect the estimated seroprevalence.

In conclusion, this study fills a gap in the global map of HSV seroprevalence data. About 85% and < 10% of the Filipino migrant population in Qatar were HSV-1 and HSV-2 seropositive, respectively, while only about 50% and < 10% of the Indian migrant population were HSV-1 and HSV-2 seropositive, respectively. While HSV-1 levels in Filipinos followed global patterns, those in Indians affirm and demonstrate an anomaly of unexplained low HSV-1 seroprevalence in Indian subcontinent populations.

Acknowledgements

We thank Ms. Adona Canlas at Weill Cornell Medicine-Qatar for her administrative support, and Ms Enas Al-Absi, Ms Rana Al-Disi, Ms Malaz Comi, Ms Malaz Elsidiq, Ms Sana Khan, Ms Layla Mohammed, Ms Mariam Nofal, and Ms Afifah Sahara at Qatar University for their support in HSV testing. We also thank Dr Asmaa Al-Marwani, Ms Maria Samatti and Ms Sana Abohasera for blood specimen collection, and the Biostatistics, Epidemiology, and Biomathematics Research Core at Weill Cornell Medicine-Qatar.

Funding: Testing kits were provided through pilot funding by the Biomedical Research Programme at Weill Cornell Medicine-Qatar. GKN acknowledges support from Qatar university internal grant, No. QUST-CHS-SPR-15/16-7 and from the Qatar National Research Fund UREP, grant number UREP18-001-3-001. LJA, SRD and MH acknowledge support from the Qatar National Research Fund (a member of Qatar Foundation) for study conception and design through NPRP grant number 9-040-3-008. The findings reported herein are solely the responsibility of the authors.

Competing interests: None declared.

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Figure 1 Overall and age-specific seroprevalence of A) herpes simplex virus type 1 and B) herpes simplex virus type 2 in male Filipino blood donors living in Qatar

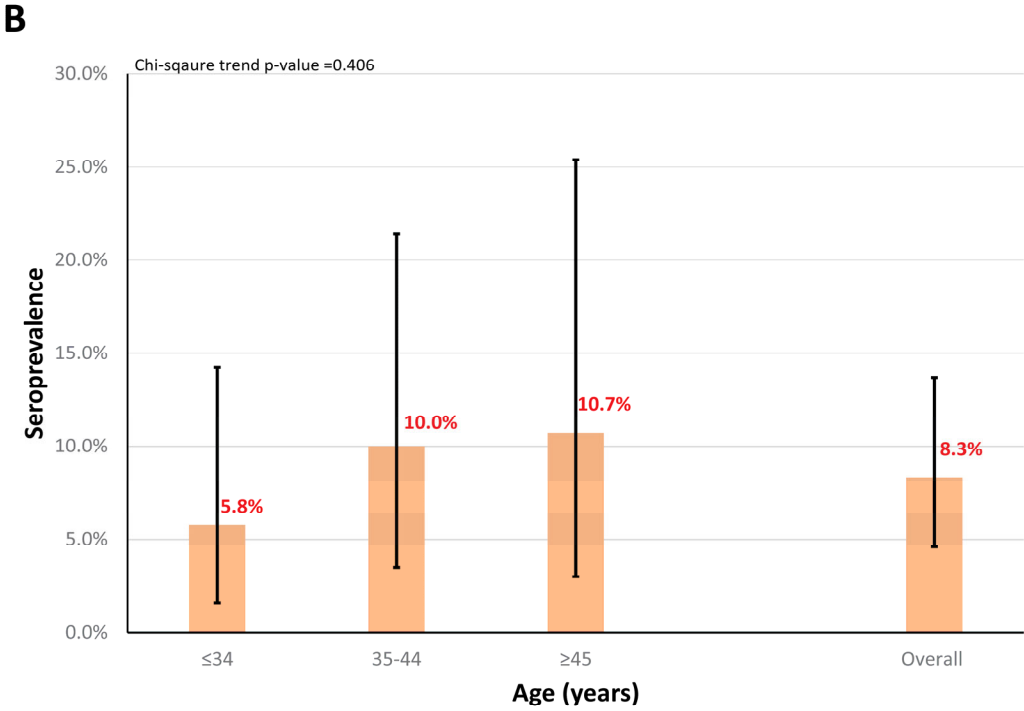
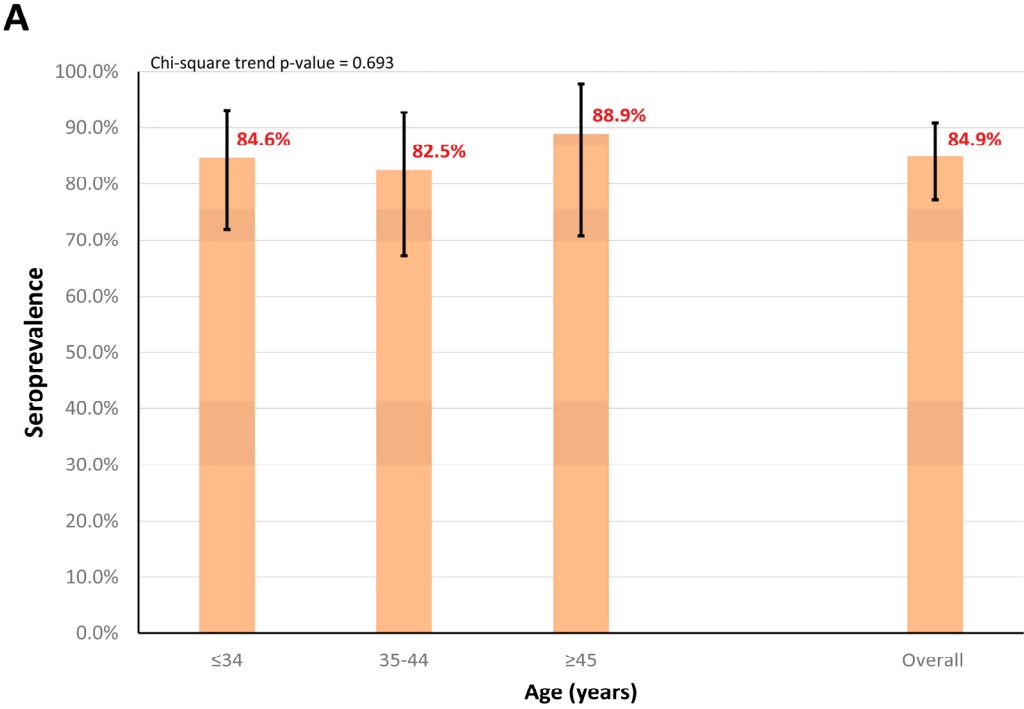


Figure 2 Overall and age-specific seroprevalence of A) herpes simplex virus type 1 and B) herpes simplex virus type 2 in male Indian blood donors living in Qatar

