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Prospective screening for monkeypox infection among men who have sex with men at an infectious diseases outpatient clinic in Copenhagen, Denmark

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Abstract

Since 2022, over 102,000 cases of mpox clade IIb have been reported worldwide, primarily among men who have sex with men. Key risk factors include human immunodeficiency virus (HIV) infection and the use of HIV pre-exposure prophylaxis (PrEP). In Denmark, the pox vaccine (Imvanex®) has been available to at-risk individuals since 2022. However, emerging cases of mpox reinfection have raised concerns regarding vaccine-induced immunity and the potential for asymptomatic transmission. This study aimed to assess the necessity of screening for mpox in an asymptomatic yet high-risk population, the majority of whom had been vaccinated. Between August and October 2023, we screened 123 PrEP users for mpox at the outpatient clinic of Copenhagen University Hospital – Amager and Hvidovre, Denmark. Polymerase chain reaction testing for mpox was conducted using rectal swabs. Among the participants, 97 had received at least one dose of the mpox vaccine. No mpox cases were detected. These findings suggest that in a highly vaccinated, high-risk population during a period of very low mpox prevalence in Denmark, asymptomatic mpox circulation is unlikely. The results support the current public health strategy of prioritizing mpox testing for symptomatic individuals and implementing contact tracing during low-prevalence periods with high vaccine coverage.

Keywords: Mpox; Vaccination; Screening; Men who have sex with men; Pre-exposure prophylaxis; Human immunodeficiency virus; Transmission

1. Introduction

Globally, there have been 102,000 confirmed cases of mpox clade IIb (formerly known as monkeypox), along with recent sporadic cases of mpox clade I reported outside Africa.[1-3] A significant rise in clade IIb cases has been noted in countries where mpox transmission

was previously uncommon, and the efficacy of antiviral treatments remains uncertain.[4,5] To date, 111 countries have reported cases, with Europe and the Americas being most affected. In Denmark, 203 cases have been confirmed since May 2022, including five new cases between June and August 2024.[6] The majority of cases have presented mild symptoms, primarily rash and fever.[7]

These recent outbreaks are marked by a notable shift in transmission patterns, with the virus now spreading primarily through sexual contact among men who have sex with men (MSM).[8-10] Furthermore, having multiple sex partners, using human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP), and being HIV-positive have been identified as significant risk factors for mpox infection with clade IIb.[7,11] Consequently, Danish authorities have offered the pox vaccine (Imvanex®) to MSM since August 12, 2022, following the World Health Organization guidelines.

Emerging data from recent outbreaks have also revealed that mpox infection in individuals with low CD4 cell counts can result in fatal necrotizing infections and that reinfection is possible in both vaccinated and previously infected individuals.[12-16] Reinfection suggests that neither natural nor vaccine-induced immunity offers complete protection.[17-19] Furthermore, reinfected individuals appear to experience fewer and milder symptoms compared to those with a primary infection.[12] This raises the possibility of subclinical infections or even asymptomatic carriage in the population.[20] Indeed, the asymptomatic carriage has been described, though no formal screenings have been performed, largely due to the high vaccination rate among those at highest risk.[21,22] If mpox is still circulating among asymptomatic vaccinated individuals, this could pose a challenge to current containment strategies.

To investigate this possibility, we conducted a screening for mpox among Danish PrEP users at an infectious disease outpatient clinic. Between August 29 and October 13, 2023, MSM who were screened for sexually transmitted infection at the infectious disease outpatient clinic at Copenhagen University Hospital, Hvidovre, were offered additional screening for mpox. Mpox polymerase chain reaction (PCR) testing was performed on rectal swabs at the Department of Clinical Microbiology, Hvidovre, using the novaplex monkeypox virus assay (Seegene, South Korea) on the CFX real-time PCR system (BIO-RAD, USA). Testing for chlamydia (*Chlamydia trachomatis*) and gonorrhea (*Neisseria Gonorrhoeae*) was performed using the Aptima Combo 2 assay on the Panther system (Hologic, USA), with samples collected from the throat, urine, and rectum. This screening was conducted as part of a quality control study of sexually transmitted disease screening and treatment.

A total of 123 MSM participated in the mpox screening. Of these, 118 (96%) were PrEP users, and five (4%) were individuals living with HIV. The median age of participants was 38.5 years. Ninety-seven (78.9%) had received at least one dose of the mpox vaccine, and 73 (59%) had received two doses. Vaccination status was assessed as of the date of testing. Six individuals (5%) tested positive for chlamydia, and 11 (9%) tested positive for gonorrhea. None tested positive for mpox. This absence of mpox cases may be due to a combination of factors: (i) vaccination-induced immunity; (ii) isolation strategies following mpox diagnosis among high-risk individuals; (iii) a generally low incidence of mpox in Denmark at the time of screening; and (iv) a high level of awareness among the at-risk population. The importance of vaccination has recently been emphasized by the 2024 outbreak in Australia, which saw over 500 confirmed mpox cases, nearly 50% of whom were unvaccinated.[23]

2. Discussion

In this screening for mpox among PrEP users, no positive cases were found. This may be due to a combination of: (i) vaccination-induced immunity; (ii) isolation strategies following mpox diagnosis among high-risk individuals; (iii) a generally low incidence of mpox in Denmark at the time of screening; and (iv) a high level of awareness within the at-risk population. The importance of vaccination has recently been emphasized by the 2024 outbreak in Australia, which reported more than 500 confirmed mpox cases, nearly 50% of whom were unvaccinated.[24]

The incidence of chlamydia and gonorrhea among the screened individuals confirms that this was indeed a population at risk of mpox infection. Although studies have demonstrated high sensitivity for mpox testing at the rectal mucosa, screening additional anatomical sites increases overall diagnostic sensitivity and can detect cases that would be missed by single-site sampling.[23,25,26] Other studies have reported that in symptomatic individuals, detection is highest in lesions and rectal swabs. While rectal swabs have slightly lower sensitivity than lesion swabs, oral and genital swabs yield even lower detection rates.[23,27] De Baetselier *et al.*[22] further identified mpox DNA in rectal and oral samples of asymptomatic individuals, with rectal swabs more frequently testing positive. As such, rectal swabs are considered among the most sensitive and reliable sample types, particularly in a high-risk, asymptomatic population such as ours. However, the exclusion of oral swabs may represent a limitation that could have led to missed cases. Still, none of the individuals screened were subsequently diagnosed with mpox.

Most participants had received at least one dose of the mpox vaccine. As vaccination may reduce symptom severity or viral load to undetectable levels, it could potentially mask true infection rates. This, in turn, could confound any association between mpox prevalence and risk behavior.

3. Conclusion

Our findings indicate that in a high-risk population, the majority of whom are vaccinated, during a period of low mpox incidence, rectal circulation of asymptomatic mpox is unlikely.

Various prospective and retrospective studies conducted at different time points during recent outbreaks have demonstrated that screening asymptomatic individuals, especially during periods of low incidence and high vaccination coverage, is not warranted, and our findings support this strategy.[20,22,28-30]

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

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Ethics approval and consent to participate

This project was conducted as a quality assurance initiative aimed at evaluating and improving internal clinical procedures. In accordance with Danish regulations, formal ethical approval was not required. Written informed consent for participation was obtained from all study subjects.

Consent for publication

Written consent for data publication was obtained from all study subjects.

Availability of data

Not applicable.

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