

Saliva As A Diagnostic Tool In Diagnosing Monkeypox In India- A Global Pandemic In Waiting – A Short Review

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Abstract:

Problem Orthopoxvirus is a genus *Variola* of the family *poxviridae* and subfamily *chordopoxvirinae*. Poxviruses are a large double stranded DNA genomes which are brick or oval shaped viruses. In humans, the infection usually occurs due to close contact with contaminated people or materials or animals. Monkeypox infection is the emerging disease which is transmitted by the virus to humans from animals, rodents and human to human transmission in people with high-risk sexual behaviour .

Materials and methods

A search strategy was designed using MesH terms and keywords specific to relevant topic.

The search included **key words** monkeypox virus, variola virus, saliva, diagnostic tool, oral symptoms, pox virus materials available only in English were retrieved

We employed in Medline (PubMed), google scholar, Scopus . Two original study regarding monkeypox were retrieved from google scholar, four review articles from PubMed , one case report from PubMed , one comparative study from PubMed, four original study from PubMed

Conclusion

Salivary diagnostic tools are noninvasive and can be cost efficient when compared to other tools, easy sample collection method, self-directed approach and non-contagious. Hence further studies are required on development and utilizing of saliva as a diagnostic tool for diagnosing the diseases in this era of infections is the pressing priority

Keywords

Diagnostic tool, Monkeypox virus, Oral symptoms, Pox virus, Saliva, Variola virus.

Introduction

Orthopoxvirus is a genus of the family *poxviridae* and subfamily *chordopoxvirinae*. Poxviruses are a large double stranded DNA genomes which are brick or oval shaped viruses. Poxviruses are known to be present throughout the world, can infect humans and other animals resulting in formation of nodules, rashes, lesions on cutaneous surfaces¹. In humans, the infection usually occurs due to close contact with contaminated people, fomites or animals. There are twelve known species in the genus, but the disease is produced by smallpox, cowpox, horsepox, camel pox, molluscum contagiosum, vaccinia and monkeypox viruses. Variola virus (smallpox) is inexistent in nature, the other viruses are still capable of causing disease to humans due to declining immunity with cessation of vaccination programs against small pox virus resulting in vulnerability to natural or man-made poxviral threats².

Human monkey pox was an endemic infection in many parts of the African continent, until in 2003 the cases of monkey pox were reported in U.S., confirming its breach from the African continent. In May 2022, several cluster of monkeypox have been reported from the nonendemic countries especially in Europe. Maximum number of cases reported are identified through sexual health or other health services². Variola virus is restricted to human host and is not zoonotic when compared to the monkey pox virus, which is why the eradication of smallpox with thorough surveillance and vaccination was possible. Variola virus still exists in two places in the world, state research centre of virology and biotechnology, Novosibirsk, Russia and the centres for disease control and prevention, Atlanta, Georgia, united states.

Monkeypox infection is an emerging disease which is transmitted to humans from animals. Evidence shows the monkeypox infection in squirrels, Gambian rodents and different species of monkeys. Infection to humans can be transmitted through bodily fluids, lesions on internal mucosal surfaces or skin surfaces such as oral cavity extending to pharynx, respiratory droplets and any fomite³. Its clinical presentation is similar to that seen in small pox in the past but less severe. Fatality in monkeypox is expected to be 1-10 percent but with proper management most patients will recover gradually. Massachusetts department of public health laboratory response network laboratory in May 2022 confirmed a case of orthopoxvirus by real time polymerase chain reaction (PCR) obtained from a Massachusetts resident. This endemic disease had caused a global health emergency in 2022 with around 20,000 cases across the globe and 6 confirmed cases in india³. In 2023 , 71 confirmed cases of monkeypox have been reported in 6 states of USA.

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research gate .Databases the mesh-compliant keywords of monkeypox virus, variola virus, saliva, diagnostic tool, oral symptoms, pox virus. We used manuscripts published from august 2009 to 20 July 2022.

Following earlier reviews, we applied the following exclusion standards.

A few examples include:

- i. Research conducted outside the time period under consideration
- ii. Presented themes outside the purview of the review;
- iii. Unpublished articles, text book references and unpublished PhD dissertations.

We incorporated all studies that complied with the requirements of scientific methodology and had relevance to any of the areas of the current review. The reviewers considered all evidence, irrespective of study design, as eligible for inclusion. The search strategy to cover all topics was established so that all evidence is mapped in the search process.

Discussion

Early disease detection is essential to reducing disease severity, preventing complications, and improving the likelihood that treatment will be effective. Due to its accessibility and simplicity, lack of invasiveness, and richness of indicators including genetic information and proteins, human saliva has received substantial importance as a potential diagnostic tool over the past few years. Current developments in the field of salivary biomarkers for the diagnosis of autoimmune diseases such as Sjogren's syndrome and cystic fibrosis, cardiovascular diseases, diabetes, HIV, cancers of oral cavity, dental caries and periodontal diseases have been vital screening tools for early diagnosis of these diseases. Salivary diagnostic tests can be offered in dental offices due to its reliability, effectiveness, usability, affordability and mainly non-invasiveness.

There are 2 clades of this virus, they are west African and Congo basin of which the Congo variant is known to cause the severe illness in humans. The incubation period of monkeypox virus is 7-17days, prodromal period lasting from 1-4 days with fever, headache and fatigue. Concomitant with rashes that develop in the presence of maxillary, cervical or inguinal lymphadenopathy in most of the cases. Enlarged lymph nodes become painful, firm and tender⁴. This typical feature is absent in smallpox infection, meaning there is a very effective immune recognition with monkeypox than smallpox, an indication that has to be further studied.

The characteristic deep-seated pustules or vesicle types of skin rash, distributed centrifugally, a well circumscribed lesion that become confluent progressing with time to a scab. Immunocompromised persons could show higher severity in symptoms. Rash appears first on the face and quickly spreads to the other body parts. Number of lesions on a patient can vary from a few to thousand⁵.

Oral symptoms

Lesions are often seen in the oral cavity leading to difficulty in drinking or eating. Indicating the earliest sign to be diagnosed in oral cavity and face. Monkeypox virus is highest rate or oral and genital shedding. A study published in Euro surveillance revealed the high viral load in all the 12 saliva samples. All patients

included were men who have physical intimacy with men, all patients reported to have more than 10 sexual partners in the previous month⁶⁻⁸.

Saliva as a diagnostic tool

The features of long prodromal period, unique immune recognition and presence of high rate of shedding of virions in oral cavity make saliva an important diagnostic tool in identifying monkey pox. The variola virus, which caused smallpox in humans, is known to primarily spread through direct contact and droplets. However, there is evidence indicating airborne transmission as well. Similarly, the highly contagious monkeypox virus has been found in significant amounts in saliva. Moreover, the nose and mouth can release viral particles through respiratory droplets, or aerosols, spittle, which could potentially accumulate in mask filters, suggesting a potential route of transmission. Screening of viral nucleic acid for the presence of virus in the oral fluid specimens for diagnosing the infection, which has proved to be more sensitive and is considered significantly less contagious as the pathogen present in the sample is in an inactive form during the initial isolation protocol of the viral nucleic acid. This is usually followed by polymerase chain reaction amplification which is relatively expensive⁹⁻¹¹. For the purpose of monitoring and evaluation of certain systemic diseases, salivary composition can play an important role in determining the level of infectious agents. The sample collection via saliva provides an easy and safe approach with less discomfort to the patient. Presence of monkeypox in the saliva is confirmed by and to contain its spread via sample collection application of salivary diagnostic tools might reflect upon a safer method to the expert technician and the patient¹².

Extensive quantities of the highly contagious monkeypox virus found in saliva suggest that transmission through saliva may play a role in sexual activity as well, warranting further investigation. As community transmission is anticipated, the spread of monkeypox to different social groups may introduce alternative modes of transmission that do not involve direct skin contact during sexual activity. These alternative pathways become more relevant and demand additional research.

Saliva as R~~T~~-T-PCR

It is possible that the monkeypox virus found in oral mucosa is contagious given that live virus was discovered in 66% of qPCR-positive saliva samples. Monkeypox viral transmission from person to person has been documented in Africa in the past, but the number of studies is small. A nucleic acid amplification test introduced by flow health announced on July 9th 2022 named monkeypox assay. Samples are collected using saliva collection kit. It will be interesting to find out if monkeypox virus may linger in saliva for prolonged periods of time. Five air samples obtained at a distance of 1-2.5m from patient beds in a hospital were found to contain modest quantities of monkeypox virus DNA, according to a 2022 study.

Further investigation is required to determine if the levels of the monkeypox virus in saliva, droplets, and aerosols are enough for efficient transmission, and to evaluate the importance of the transmission through saliva and respiratory pathways in the disease's spread within the community.

Conclusion

A changing world with advancing technology and medicine, yet living in an era with a pandemic emerging out every other day makes it a contradictory approach. In spite of advances in technological development with improved health measures, combating the pandemic of these diseases has become perplexing in numerous ways. To come to an end of Covid-19 seems to be a beginning to several viral disease like monkeypox. Saliva being the fluid known to have high diagnostic value with high sensitivity and specificity can be a major breakthrough of the future. Today the healthcare workers and the population would look upon a noninvasive technology to perform a test in comparison to throat swab or skin lesion swabs and biopsy. Salivary diagnostic tools are noninvasive and can be cost efficient when compared to other tools, easy sample collection method, self-directed approach and non-contagious. Hence further studies are required on development and utilizing of saliva as a diagnostic tool for diagnosing the diseases in this era of infections is the pressing priority.

Ethical statement: ethical clearance and informed consent is not applicable

Competing interests

No competing interests were disclosed.

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