



Human Monkeypox- An Update

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Received:

15.08.2022

Accepted:

25.08.2022

Published:

25.08.2022

Keywords

Human
monkeypox
disease,
Monkeypox,
Orthopoxvirus,
Poxviridae,
Smallpox.

ABSTRACT: Human monkeypox disease, a rare zoonosis endemic in Western and central Africa emerged in 56 different countries around the world with an increase of 77% in cases is a global concern. Natural animal reservoir of monkeypox virus is still unknown; rodents and primates except human are the probable source of virus introduction to human. A clear and sufficient data about the virulence and transmissibility of human monkeypox disease is limited due to inconsistency in the epidemiological studies. As per World Health Organisation and Centre for Disease Control status report smallpox vaccine is found to provide 85% immunity against human monkeypox disease. There is currently no specific treatment available and two antibiotic drugs tecovirimat and brincidofovir can be used as supportive treatment for time being. © 2022 iGlobal Research and Publishing Foundation. All rights reserved.

INTRODUCTION

Human Monkeypox is a zoonotic disease caused by monkeypox virus belonging to Orthopoxvirus genus under Poxviridae family. As the name suggests the first monkeypox virus was isolated from monkeys in 1958 at Statens Serum Institution, Copenhagen [1,2]. First case of human monkeypox was recorded in 1970 in Democratic Republic of Congo where the outbreak of the disease occurred in rural rainforest of West Africa and Congo basin [3]. The smallpox virus (variola virus) is closely related to monkeypox virus and the vaccination against smallpox was reported to be 85% protection against monkeypox disease. Other than monkey, rope squirrels, Gambian pouched rats, and dormice are competent host of monkeypox virus [4]. The first transmission of this pox virus to human was by their encounter with the infected animal [5]. After 1970, 81 cases of human monkeypox were reported in United States in 2003. In 2017 human monkeypox became a large outbreak in Nigeria in an 11 year old boy and till November 2017, a total of 146 cases were reported [6]. In 2022 from early May, the cases of human monkeypox disease started to appear in different countries outside central and West Africa where it is endemic. Till 10 August 2022, a total of 27,814 cases were reported with 11 deaths in 89 countries around the world [7]. As per WHO (World Health Organisation) third report on multi-country outbreak of human monkeypox disease, 10 countries that recorded highest

number of cases includes; USA with 7510 cases is on the top of the list, Spain reported 4577 cases, Germany reported 2887 cases, United Kingdom reported 2759 cases, France reported 2239 cases, Brazil reported 1721 cases, Netherland have 959 cases, Canada have reported 957 cases, Portugal reported 710 cases, and Italy is the last in this list with 505 cases [8,9]. These 10 countries account for 89% of total human monkeypox disease [9].

EPIDEMIOLOGY AND TRANSMISSION OF HUMAN MONKEYPOX DISEASE

Human monkeypox disease epidemiology was first collected from cases reported in 1980. According to these reports the case fatality rate of these disease were reported to be 17%, the rate of secondary attach was 3.3% and the secondary transmission was reported to be 9% [10]. In comparison to small pox the transmission rate of human monkeypox was low and it was not considered serious public health problem and there was no evidence found of its sustained transmission in human. From 1980 to 1986 after the study of 13 cases it was found that the transmission is very low. US Centres for Disease Control and Prevention (CDC) and WHO from 1986 upto 1997 reported 419 cases and analysis of these cases result showed high transmission of the disease upto 78% [11].

Cite this article as: Khan, J. Human Monkeypox- An Update. Indo Global J. Pharm. Sci., 2022; 12: 248-252. DOI: <http://doi.org/10.35652/IGJPS.2022.12032>

The reports of CDC and WHO have given good information about hosts and reserves of the viruses which includes squirrels, non-human primates, and rats as primary hosts [12]. The infection in these animals were reported to occur under natural conditions and many other serological studies found that the transmission of the virus to human may have taken place through *Funisciurus anerythrus* (squirrels) as these squirrels stay near agriculture areas and human settlements [11]. The laboratory testing and PCR (Polymerase Chain Reaction) reports of samples from *Funisciurus spp.* reported high seropositivity of monkeypox virus [13]. No study till now identified any definite reservoir or host for MPV (Monkeypox Virus), but primates other than human and rodents were found to be possible natural reservoir related host of this virus. Due to such large population of natural reservoir it becomes difficult to study the host-pathogen interaction, effect of ecological and climate change on MPV virus, and the nature of virus. MPV virus does not have any specific tissue tropism as it is found in large number of tissues.

Regarding the transmission of MPV as per the report of CDC in 2003 mentioned the symptoms of the disease including fever, unexplained rash with onset of symptoms after 21 days of exposure to disease or infected animals or human. Symptoms other than fever and rashes reported to be chills, sweats, headache, backache, lymphadenopathy, sore throat, cough, and shortness of breath. The rashes first may locate on or near genital organs (vagina, penis, testicles, and labia) or around anus then spread to other areas of body including hands, feet, chest, face and mouth. The rash shows many stages of development including size of pimples or blisters, and scabs formation before healing [14]. These blisters may be painful and itchy. The human monkeypox disease starts with flu like symptoms after 3 weeks of exposure and the rashers starts appearing after 1 to 4 days [15,16]. The patient with this disease can spread it from the time of its symptoms appear till the rash heal and the new skin has formed. From first symptom to complete healing the illness lasts from 2 to 4 weeks (**Figure 1**).

The transmission of MPV includes exposure to exotic or wild mammalian pets that are living in household, petting, or visiting vet clinics. According to the new report released by WHO on 7 August 2022, transmission of MPV in human population through sex, which is 73% of total positive cases. From these cases 99% of the cases were reported to be in males with a median age of 36 years [17]. The biggest number of males cases reported was identified as gay, bisexual men who had sex with other men or have sex with other multiple partners. The symptoms as per WHO that the countries on high alert should look includes; atypical rashes that progress in sequences from macules, papules, vesicles, pustules, scabs in all areas of the body with fever, inflamed lymph nodes, muscle pain, and back pain. The confirmed patients should be isolated until the lesions are crusted, the scab fell off and a

new layer of skin is formed to be considered fully recovered [18].

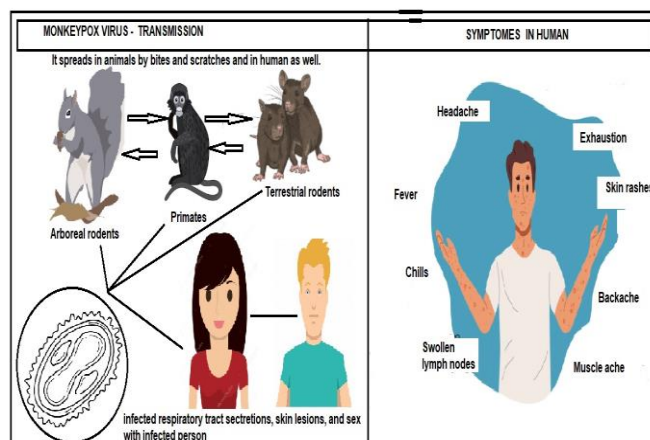


Figure 1: Transmission of monkeypox from animals to human and from human to human and symptoms of disease.

DIAGNOSIS

Diagnosis of monkeypox from a clinical sample depends on the combination of clinical and epidemiological information of the patient with the history of vaccination. The specimens collected from lesion swab or crust contains stable viral DNA (Deoxyribonucleic acid) that can be stored for a long period in dark and cool environment [19]. Other than lesion the samples that can be considered for diagnosis includes skin biopsy tissue and blood samples. Skin samples can be used for histopathological test [20]. The lesions in human monkeypox are distinct from smallpox based on the necrosis of stratum basale, stratum spinosum, and adjacent dermal papillae. Electron microscopic study of the lesion shows many large brick shaped Orthopoxvirus particles in the cytoplasm of epidermal cells of the lesion [21].

Different techniques used for identification of MPV include electron microscopy, immunohistochemistry, real time PCR, and ELISA (Enzyme-Linked Immunosorbent Assay). Single identification Anti-Orthopoxvirus immunoglobulin G (IgG) will not give definite diagnosis for patient who have been exposed to Orthopoxvirus by vaccination during their lifetime and serological assay for anti-Orthopoxvirus immunoglobulin M (IgM) is found more appropriate for MPV diagnosis [22].

With the experience of COVID-19 (Coronavirus disease-19) and need for fast detection methods and on the basis of recommendation from WHO for PCR test as fast and accurate method of diagnosis, different companies around the world are working to develop testing kits [23]. Following table includes information of different kits now available for testing MPV (**Table 1**).

Table 1: Different type of Monkeypox Virus testing kit available in market.

Name of Kit	Type of Kit	Manufacturer	Sample type	Time to show result	Target
Bioperfectus Monkeypox virus Real time PCR kit	Real time PCR	Jiangsu Bioperfectus technologies Co., Ltd China	Human tonsillar swab, nasopharyngeal swab, serum, whole blood lesion	60 min	F3L gene
Creative Biogene Monkeypox virus real time PCR kit		Creative Biogene, USA	Serum and lesion exudate	120 min	DNA
VIASURE Monkeypox virus real time PCR kit		Certest BIOTEC S.L Spain	Serum vesicle cutaneous skin fluid, wound swab	120 min	DNA
XABT Monkeypox Real time PCR Kit		Beijing Applied Biological Technologies Co., Ltd	Nasal swab, Oropharyngeal swab, sliva, urine, skin lesion tissue exudate and blood	120 min	USA
Genekaim Monkeypox real time PCR kit		Genekam Biotechnology AG, Germany	Nasal swab, sliva, urine, skin lesion tissue exudate and blood	120 min	DNA
JOYBio's Monkeypox Antigen Rapid Test kit	Lateral Flow kits	JOYSBIO, China	Lesion swab, Whole blood, Serum, Plasma	20 min	IgG/IgM
VivaDiag Monkeypox virus Rapid test kit		Vivachek, Biotech Co., Ltd	Lesion swab, Whole blood, Serum, Plasma	20 min	IgG/IgM
AIVD Monkeypox virus Rapid test kit		Shenzhen AIVD Biotechnology Co., Ltd. China	Lesion swab, Whole blood, Serum, Plasma	15 min	IgG/IgM

CLINICAL MANAGEMENT, VACCINATION AND TREATMENT

After ten years of appearance of first case of human monkeypox disease in 1968, some researchers reported 85% immunization against the disease by smallpox vaccine. On the basis of analysis of 215 cases, CDC recommended smallpox vaccination for research investigators, health care workers, animal- control caretakers, caretakers of infected patients, and veterinarians [24]. A suspected case can be identified on the basis of following criteria;

A person was having travel history to affected countries within last 21 days showing with an unexplained acute rash and signs or symptoms like; swollen lymph nodes, fever, headache, body aches, profound weakness. A person having these characters is considered as clinically compatible illness and have epidemiological link with contaminated materials of infected parents like clothing, bedding, utensils, skin to skin contact etc. After identification surveillance strategies should be adopted so as to isolate cases to prevent further transmission, to provide clinical care, identification and mange contacts, protect frontline health workers, and effective control and preventive measures based on route of transmission [25].

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The use of post exposure smallpox vaccine was suggested by CDC to be used in people had direct exposure within 4 days and with 2 weeks of recent exposure as the result of smallpox vaccine in post exposed people were found effective. In 3rd external report by WHO also recommended the use of smallpox vaccine in the current situation as primary preventive vaccination before the exposure including high risk group's especially gay, bisexual men having sex with multiple partners, laboratory specialists working with orthopoxviruses and testing monkeypox, and outbreak response team [25]. As per the WHO guideline, all affected countries should start vaccination program and information campaigns as fast as possible. After vaccination it takes 2 weeks to develop full immunity but it can be affected by different circumstances that need to be identified for this outbreak. The data collected on the basis of vaccination and alternate treatment should be used to generate information regarding the outbreak control system.

On May 17, 2022 WHO and CDC recommended the use of JYNNEOS and ACAM200 vaccines during monkeypox outbreak in United States. The guidelines to use these vaccines are released by CDC's Advisory Committee on Immunization Practices (ACIP). According to ACIP JYNNEOS vaccine is approved for preventing both smallpox and monkeypox disease and ACAM2000 vaccine is approved smallpox disease but under Expanded Access Investigational New Drug (EA-IND) protocol it is also made available to be used against monkeypox disease. JYNNEOS should be administered subcutaneously in an injection of volume 0.5mL. People can be vaccinated after exposure to monkeypox virus to prevent the disease. At present no data is about the efficacy or effectiveness of ACAM2000 in current outbreak. The supplies of JYNNEOS are limited around the world and ACAM2000 is available but reported to have many side effects [26].

As no specific treatment for human monkeypox disease is approved till date so antiviral medications such as cidofovir, tecovirimat and brincidofovir that was used to treat smallpox can help patient of monkeypox infection. WHO and CDC is asking for feedback on target product profile (TPP) therapeutics on MPV cases from experts from different fields of research, industries, drug product developers, national and international infection control clinicians and personnel involved in management and control of MPV disease.

CONCLUSION

During early 1970s intense vaccination program around the world helped in eradication of smallpox but by the end of this year a new human monkeypox virus disease caused by virus of Orthopoxvirus family was discovered. Before April-June 2022 monkeypox disease was limited to West and Central African countries but till August now it is present in Regions of America, European region, Eastern Mediterranean region, Western Pacific region, and African regions. From 2019 world is already struggling with COVID-19 pandemic and re-occurrence of MPV disease will make the situation more difficult in all aspects of life. The lessons learned during the

COVID-19 like management and control strategies with fast developed awareness programs can be used to handle this situation and it can be controlled in a better way. Development of rapid diagnostic methods including point of care testing will help to limit potential outbreak. Better understanding about virus family, animal reservoirs, and human disease from pox family will guide to develop preventive strategies control of human monkeypox disease.

ACKNOWLEDGEMENT

Authors would like to express a special thanks to Majmaah University for providing facilities and resources to carry out an extensive literature survey on the presented topic.

AUTHOR'S CONTRIBUTION

Manuscript was prepared, revised and submitted by JK.

ETHICS STATEMENT

The authors have taken all the necessary permissions as per ethical guidelines wherever applicable. The authors will be responsible for all the technical content mentioned in the manuscript. Journal and Publisher will not be responsible for any copyright infringement and plagiarism issue.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY

Not declared.

FUNDING SOURCE

No external funding source has been disclosed.

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Indo Global Journal of Pharmaceutical Sciences (ISSN 2249 1023; CODEN- IGJPAI; NLM ID: 101610675) indexed and abstracted in CrossRef (DOI Enabling), CNKI, EMBASE (Elsevier), National Library of Medicine (NLM) Catalog (NCBI), ResearchGate, Publons (Clarivate Analytics), CAS (ACS), Index Copernicus, Google Scholar and many more. For further details, visit <http://iglobaljournal.com>