Editorial

Monkeypox: A Global Concern

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Monkeypox (MPX) is a zoonotic disease caused by the Monkeypox virus (MPXV).[1] Monkeypox virus has a similarity with smallpox virus. It is an enveloped double stranded DNA virus belonging to Orthopoxvirus genus of the Poxviridae family. Though MPX virus is a DNA virus, major and frequent changes in the genetic structure are less likely.[1]

Transmission of the disease occurs from animals to humans and humans to humans following close contact. The natural reservoirs are monkeys, squirrels, Gambian pouched rats, dormice, nonhuman primates, and other species. Humans may be infected by bite, scratch, close contact or by eating inadequately-cooked meat of infected animals. Transmission between humans occurs by large respiratory droplets, direct contact, and through contaminated fomites. The secondary attack rate among household contacts is less than 10%, unlike smallpox where it was 35–88%.[2] The role of direct sexual transmission is uncertain, but intimate skin and mucosal contact during sex facilitates spread. Vertical transmission from mother to fetus or newborn leading to congenital MPX has also been reported. Vertical transmission of monkeypox can lead to fetal infection. In a series of four pregnant women from Democratic Republic of Congo (DRC) with monkeypox, two had early miscarriages and one had a second-trimester fetal loss.[3]

The first human case reported was in 1970 in a child in DRC.[4] Since then, monkeypox is endemic in Central and West Africa and two distinct clades have emerged—the Congo basin or Central African clade (clade 1) and the West African clade (clade 2). The former is more virulent with higher case fatality.[5] On 6 May 2022, a case of monkeypox was reported from the UK in a traveler who had returned from Nigeria.[6] Since then, the number of cases have increased exponentially and in people with no history of travel to endemic areas. In the period between 1 January 2022 and 22 July 2022, 16,016 laboratory confirmed cases of monkeypox and 5 deaths have been reported to WHO from 75 countries/territories/areas in all six WHO regions.[7] The case fatality ratio is around 3-6%.[8] Considering the increasing number of cases across the world, the WHO declared MPX as a public health emergency of international concern (PHEIC) on 23 July 2022.[9] Re-emergence of monkeypox in endemic and nonendemic areas has been attributed to changing biologic nature of the virus, climate change, waning immunity following cessation of smallpox vaccination coupled with increased international travel following the lifting of COVID-19 restrictions and high-risk sexual activity.[10] While it is true that at this time mainly adult homosexual males have been affected, the illness is likely to spread into the general population, women and children. Health care workers are at a higher risk for infection. There is also concern about humans infecting animals, which may then serve as a recurrent source of infection.[11]

The incubation period ranges from 5 days to 21 days, typically 6–13 days.[12] All ages are affected but the median age has shifted upwards with passage of time.[13] Men are more affected than females. Clinical features are similar to that of other pox virus infections including smallpox.[14] The prodromal phase is nonspecific and lasts generally for 0–5 days. The disease is characterized by a short febrile illness, headache, lethargy, myalgia, with lymphadenopathy followed by a rash which spreads centrifugally and passes through phases of macules, papules, vesicles, and pustules. The lymphadenopathy appears with onset of fever and may be unilateral/bilateral cervical, axillary, or inguinal. This is followed by the appearance of the rash which lasts for 2–4 weeks. The lesions are polymorphic and painful till they become

crusted.[15] Recovery occurs in most patients within 2–4 weeks. Complications are more likely in children, pregnant women, and the immunocompromised persons.[12,15] Factors that predispose to severe illness include younger age (children), underlying immune deficiencies including HIV infection and other chronic illnesses, and absence of previous smallpox vaccination. The complications include secondary infections, bronchopneumonia, sepsis, encephalitis, and involvement of the cornea with ensuing loss of vision. The case fatality rate ranges from 1% to 10% and varies with clade (discussed earlier), host factors, vaccination status, and access to care. In a case series of 282 patients from DRC, there were no deaths in people who had received smallpox vaccination, but was 11% in those unvaccinated.[16]

Laboratory diagnostics are principal components for identification and surveillance of disease. The various laboratory methods available for diagnosis include viral isolation, immunohistochemistry in tissues, molecular diagnosis, electron microscopy, and serology. The molecular tests include RT-PCR, recombinase polymerase amplification (RPA), loop-mediated isothermal amplification (LAMP) technology, and restriction-fragment-length polymorphism (RFLP), etc. Real-time PCR (RT-PCR) test on samples obtained from skin lesions, throat, blood, and urine can be used for diagnosis of MPX with good sensitivity and specificity. However, these tests are expensive and not available commercially. Specific IgG and IgM against MPX may be detected by enzyme-linked immunosorbent assay (ELISA) after 5 and 8 days of infection. New tests are needed for a more precise and rapid diagnosis.[17]

Treatment is largely symptomatic. Treatment of MPX is symptomatic and supportive including maintaining fluid and electrolyte balance, nutrition, symptomatic therapy with antipyretics/analgesics, early identification of secondary infections, and prompt treatment with appropriate antimicrobial agents.[18]

Considering the fact that most cases of monkeypox are self-limiting, no specific antiviral therapy is indicated. Antiviral therapy may be considered in patients with severe and progressive disease, in the severely immunocompromised and in pregnant women, for high-risk groups, health care workers, and close contacts. Control of the monkeypox outbreak needs a multipronged effort comprising enhanced surveillance, quick diagnosis, isolation of affected people, ring immunization, and adoption of "one health" approach.[12,17]

There are limited antiviral drugs available for MPX. Cidofovir which acts by inhibiting the viral polymerase has in vitro activity against pox viruses. It is, however, very nephrotoxic. Brincidofovir (CMX-001) is modified cidofovir with lesser nephrotoxicity. However, no convincing benefit was reported with three UK MPX patients with brincidofovir.[19] Recently, the compound ST-246 or tecovirimat has been approved for treatment of orthopox virus infections including smallpox, cowpox, monkeypox, and vaccinia in USA, Canada, and Europe.[20]

Antivirals have been used anecdotally in the management of MPX in the nonendemic countries. In a recent study, only 5% of the patients received antiviral therapy (2% intravenous/topical cidofovir, 2% tecovirimat, and < 1% vaccinia immunoglobulin). The patient with severe epiglottitis improved rapidly after giving tecovirimat.[21]

New therapeutics and vaccines offer hope for the treatment and prevention of monkeypox; however, more research must be done before they are ready to be deployed in an endemic setting. There is a need for more research in the epidemiology, ecology, and biology of the virus in endemic areas to better understand and prevent human infections.[22]

It has been documented that those individuals who had received smallpox vaccine were better protected against MPX or developed less severe illness as compared to those with no history of smallpox vaccination.[23] Hence, smallpox and modern modifications of smallpox vaccine have been recommended for protection against MPX, though the efficacy is uncertain and needs validation.

These vaccines are currently not recommended for mass administration. They are recommended for post-exposure prophylaxis preferably within 4 day/ maximally 2 week of exposure and for pre-exposure prophylaxis in high-risk individuals including health care workers.[24] Prior smallpox vaccination gives partial protection against monkeypox. The steady increase in monkeypox cases in Africa over the past few decades were ignored by the global scientific community till this year, when more than 16,000 cases have been reported from nonendemic countries. Monkeypox has recently been labelled as a public health emergency of international concern by the WHO. While most of the current cases are in men who have sex with men, there is the larger threat of the disease spilling into the general population.[12]MPX has been declared a global emergency and the disease burden will increase. Clinicians should maintain a high index of suspicion for this disease and follow the protocol for diagnosis, reporting, and isolation of the cases, and allay anxiety and misconceptions in the public. While it is the disease in the nonendemic countries that has gathered world attention, focus should be on controlling the disease in Africa where most of the deaths continue to occur. The lesson for the future is to not ignore neglected tropical diseases. In the current age of globalization, "no one is safe unless everyone is safe".[25, 26]

Prof. Chaklader Md. Kamal Jinnah
Department of Biochemistry
North Bengal Medical College, Sirajgonj
Email: cmkjinnah30@gmail.com

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