Metanalysis of Vaccine Efficacy for Monkeypox According to Clinical Criteria of History Taking, Clinical Features and Laboratory Investigation

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Systematic Review Article

ABSTRACT

Monkeypox virus is DNA virus of Orthopoxvirus. The Monkeypox is zoonosis disease first diagnosed in the Democratic Republic of the Congo in 1970 and originally transmitted from Vertebrate Reservoir. In 1796, Edward Jenner was the first physician achieved vaccine and prove its efficacy through exposing James Phipps to smallpox after immunization. The current study revises the vaccine efficacy and mortality rate of monkeypox. It is mainly transmitted from Squirrels to human and cause mortality rate ranging from 2.7 to 10.1%. Globally, it estimated 4.4% the mortality rate of Monkeypox cases. Based on current review study, the effectiveness of smallpox vaccine in preventing the monkeypox is quite variable due to several selective clinical cases criteria such as history taking and clinical features and laboratory investigation, which modify the statistical result of the vaccine efficacy. The current study clarifies the faults of calculation by eliminating several reasons and estimating the effectiveness of vaccine in the household and find it to be 16.3% whereas total Vaccine efficacy is 0.6%. Using preventive measures are the first line to avoid infection therefore healthcare workers must adhere to infection control precautions. A current study warns scientists to create monkeypox vaccine rather than depending on smallpox vaccine effectiveness due to lacking of current vaccine effectiveness evidence and treatment.

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1. INTRODUCTION

Monkeypox virus is a double stranded DNA virus of Orthopoxvirus genus of Poxviridae family [1]. The first case of Monkeypox virus diagnosis was in cynomolgus monkeys in a laboratory setting in Copenhagen, Denmark in 1958 [2]. Later, the first human case was diagnosed in nine months child in the Democratic Republic of the Congo in 1970 [2]. In animals, there are different Vertebrate Reservoir in which Squirrels are found to be the main reservoir. In 1796, Edward Jenner was the first treating physician achieved vaccine through exposing James Phipps to smallpox after immunization [3]. The current review study discussed the vaccine efficacy and mortality rate of monkeypox. The world health organization has reported twenty-eight suspected and ninety-two confirmed cases of monkeypox in 12 non-endemic countries in May 21 [4]. In August 2022, monkeypox cases were distributed over eighty-seven countries globally recording above 25,000 confirmed ones [5].

2. METHODS

The literature linked to monkeypox are attained from PubMed and Google Scholar database. On PubMed, there are 89 articles and on google scholar there are 1300 articles. All the article published in 2020 were found to be almost 390 hundred. The entire article were found and selected based on the keyword 'Smallpox, Orthopoxvirus, Poxviridae, Mortality, Edward Jenner and monkeypox virus. The articles were selected only in English language. The data were collected and analyzed via Statistical Package for the Social Sciences (SPSS).

3. RESULT

The current study reviews 10980-suspected cases, which include 1504 confirmed cases. It includes revision of different studies of different countries Cameron, Central African Republic, Democratic Republic of the Congo (DRC), Democratic Republic of the Congo (DRC) and Nigeria. The current studies estimated the death rate range from 2.7% to 33.3% with the correct global mortality rate of confirmed cases 4.4% (Table 1).

4. DISCUSSION

Monkeypox case diagnosis in the Democratic Republic of the Congo in 1970 [2] in which transmission was mainly by Squirrels. The monkeypox is zoonosis disease which can be transmitted from human to human, too. In 97 animal cases study, monkeypox virus found to be in African Rope Squirrels in 26.8% whereas Squirrels West Africa Democratic of Republic Congo (DRC) in 19.59%. Further, the transmission of monkeypox from Gambian Giant Rat Africa and Midwest US (Wisconsin) in 15.46% and Gambian Sun Squirrel (*Heliosciurus spp.*) in DRC 7.22% whereas Sooty Mangabey (*Cercocebusatys*) in 5.15% and Dormice Africa in 5.15%. In addition, the transmission of monkeypox from Prairie Dog Indiana (Wisconsin) and "Bushmeat" found to be in 3.09% whereas in Giant Anteater, Giant Pouch Rat and Thomas's Rope Squirrel (*F.anerythrus*) it founds to be 2.06%. Yet, the transmission of monkeypox from Hedge Hog Africa, Jerboa Africa, Opossum Africa, Woodchuck Africa, Antelope, African Civet, Cricetomys and Graphiurus in 1.03%. Therefore, the most responsible reservoir is squirrels. The virus has direct contact transmission in 83.33%, aerosol in 8.33% and fomite in 0.33% [6]. It may be transmitted from the animal to humans (primary zoonotic transmission), from humans to humans via bodily respiratory droplets, fluids such as blood, salivary skin lesion [7,8]. A series studies support transmission through sexual intercourse [9-12] which reach up to 83% of transmission monkeypox cases via gay or bisexuality [12].

The clinical manifestations of monkeypox includes headache, fever, chills, sore throat, rashes (macular, popular vesicular, pustular), lymphadenopathy, myalgia, back pain, generalized malaise [13-15]. According to the incidence of clinical features, rash (97%), fever (85%), chills (71%), lymphadenopathy (71%), headache (65%) and myalgias (56%) [16]. In 1796, Edward Jenner was the first treating physician prove the efficacy of the vaccine by exposing James Phipps to smallpox after immunization [3]. World Health Organization stated that the Smallpox vaccine has effectiveness in preventing monkeypox almost 85% according to revision of study done by Fine et al [7]. Fine and his team collected suspected 834 cases including 598 vaccinated and 236 unvaccinated cases among which 36 confirmed monkeypox cases including 10 vaccinated and 26 unvaccinated cases. Therefore, the attack rate of vaccinated and unvaccinated group is 0.017 and 0.110 respectively. According to

practical guide for doctors, nurses, laboratory technicians, medical auxiliaries, and logisticians [17], the vaccine efficacy usually calculated by three methods (Fig. 1).

Based on the first method, the vaccine efficacy is a result of [(0.110-0.017) \0.110]x100 = [(0.093)\0.110] x 100 = [0.85] x100=85%

Based on the second method, the vaccine efficacy is a result of 100-(598-10)\ 598(1-10) =100-588\ 598(9) =100-(588\5382) = 100-10.9 (100-10.9) = 89.1% which mention as second vaccine efficacy for extradomiciliary contacts

Based on the third method, the vaccine efficacy is 85%, which is a result of (1- risk ratio "RR") x100= 1-(0.110-0.017) x100= (1-0.15) x100=0.85 x100= 85%

Therefore, the use of three different epidemiological methods reached the accurate percentage of 85% of smallpox vaccine efficacy to prevent monkeypox stated by the World Health Organization based on fine et al [7] study. The main important questions regarding vaccine efficacy are clinical questions must be raised in the current study. The vaccinated and unvaccinated groups were selected based on present and absent of scar in Fine et al [7] study. How the collector of sample differentiates the smallpox vaccine scar from other vaccine scar such as Bacillus Calmette-Guerin (BCG). In 1964, 18 experts from the World Health Organization work to control the infection by estimating the price of BCG vaccine in Zaire [18]. In Zaire, health services encouraged vaccination. Between 1971 and 1972, 1030709 smallpox and 214832 BCG vaccinations were performed respectively which double and ten time greater than number of vaccinations have been given during the period 1968-1970. (Zaire: Smallpox Cases by Month, (1968-1971) reported by the World Health Organization [19]. In addition, study done by Arita et al [20] stated a rising reports of monkeypox cases with coexistent scar indicating vaccination. Moreover, Fine et al [7] assumed 70% of vaccinated group received vaccine based on a history of vaccination in the past whereas Jazek et al [21] did not estimate the vaccine efficacy. The previous reasons hesitate the 85% vaccine efficacy clinically.

The history is not enough because the language barrier and low education found to be in rural area. The scar may indicate vaccination either smallpox or BCG immunization. Although, Smallpox is self-limited disease, which provide permanent immunity, the vaccinated and unvaccinated group may develop the infection with lack of laboratory work evidence and deficient material therefore the most of monkeypox cases diagnosed clinically rather than laboratory evidence in 1970s. Several concerns may arise regard method of collecting sample based on either the history or scar presentation as evidence of contact and vaccination.

In another study reported by Jezek et al [22] in Zaire between 1981-86, the data classified into vaccination and non-vaccination based on the presence of the scar as well as the contact based on living and nonliving persons which are a total of 338 monkeypox patients out of 3686 contacts and infection rate found to be 12.7% of total number on Table 1. In the current study, more details were looked for to find the infection attack rate of 2657 vaccinated and 1029 non-vaccinate based on 43 and 295 vaccinated non-vaccinated infected of 388 found to be 1.62 and 28.7%. Based on vaccine efficacy formula, it found to be 94.4%. After revision of Jezek et al [22] study, he stated the secondary infection rate of affected village in vaccinated and unvaccinated group based on the scar found to be 0.96% and 7.47% whereas the vaccine efficacy rate is 87.2% based on current study calculation. In affected houses, the secondary infection rate in vaccinated and unvaccinated group was found to be 1.01% and 7.71% whereas the vaccine efficacy rate is 86.9%. Surprisingly, the unvaccinated people who are living in neighboring house had less risk of infection than person living in other houses. Neighboring house may and may not have same contact risk to infected vaccinated or unvaccinated people. Therefore, the affected houses will provide more accurate infection rate and vaccine efficacy than the affected village. The previous percentages have not considered in Jezek et al [22] whereas only calculated in current study based on deficient points found in study method. Further, Jezek et al [22] study described that the sample collector in several visits every 7 to 10 days done by nurses and health inspectors who have less experience in history taking and clinical examination compared to physicians beside the duration may create missing information between visits. Furthermore, the incubation period is ranging from 5 to 21 days and the typical incubation period of monkeypox virus infection is usually from 6 to 13

days [1,5,19,25] therefore the missing data can be occurred due to the short duration of visit in history or clinical examination. Also, the test is done by:

$$\textbf{1} \quad \text{Vaccine efficacy} = \frac{NVAR - VAR}{NVAR}$$

$$\textbf{2} \quad \text{Vaccine efficacy} = \frac{PPV - PCV}{PPV \times (1 - PCV)}$$

$$\textbf{3} \quad \text{Vaccine efficacy} = (1 - RR) \times 100$$

$$RR = \frac{VAR}{NVAR}$$

Fig. 1. Vaccine Efficacy estimation methods
VAR: Attack Rate of Vaccinated, NVAR: Attack Rate of Unvaccinated, PPV: Percentage of Population Vaccinated, PCV: Percentage OF Cases Vaccinated, RR: Relative risk

The World Health Organization Collaborating Centers for Disease Control in Atlanta, USA, and at the Research Institute for Viral Preparations in Moscow, skin sample examined by electron microscopy and cultured on chicken embryo chorioallantoic membrane and in tissue culture and serum sample. Specially, Anti-orthopoxvirus IgM indicates recent infection while IgG indicate either previous infection or vaccination [23].

Therefore, serum sample were to detect antibody, which may indicate previous infections or vaccination, which hesitate the result of investigation in deciding infection, rather than vaccination.

In addition, Jezek et al [22] stated the secondary infection rate of vaccinated and unvaccinated group was found to be 1.31% and 9.28 respectively whereas the current study found the vaccine efficacy rate 85.9%. The vaccination efficacy of age groups (0-4 years), (5-19 years), (10-14 years) and above 15 years found to be 100%, 80.4%, 90.3% and impossible to determine the percentage respectively. The selection of vaccinated people cases based on the scar present which can be Bacillus Calmette-Guerin vaccine rather than smallpox vaccine. The peak of vaccine efficacy found to be 4 years and below when the vaccinated group is zero. Therefore, vaccine efficacy is inaccurate and incomparable to other age groups. Five to nine and ten-to- fourteen-year groups, the vaccinated group including two and one in number respectively that may provide misleading in infective attack rate and accuracy of vaccine efficacy.

Jazek et al [21] did not estimate the vaccine efficacy of affected houses of vaccinated and unvaccinated members due to small number of participants whereas the current study estimated 72.7% vaccine efficacy.

Table 1. Monkeypox mortality rate are variable in different countries

Country	Suspected Cases	Confirmed	Death	Rate %
Cameron*	25	3	2	8
Central African Republic (CAR)*	6	6	2	33.3
Democratic Republic of the Congo (DRC)* 2020	6 216	222	-***	3.6
Democratic Republic of the Congo (DRC)* 2021	3 091	83	-***	2.7
Democratic Republic of the Congo (DRC)* 2022	1 152	1 152	55	4.7
Democratic Republic of the Congo (DRC)*	138	-***	14***	10.1
Nigeria 2021	98	34	0	0
Nigeria 2022	13	4	0	0
Nigeria**	241	241	8	3.3
Total		1504	81	
The correct global mortality rate of confirmed cases	10980	1504	67	4.4%

European Centre for Disease Prevention and Control. Monkeypox multi-country outbreak [4].
**World Health Organization - Regional Office for Africa (WHO/AFRO) [26].
Nigeria Centre For Disease Control (NCDC) [27].
*** Note: to in case of the study has no resources of confirmed cases and death, the number is corrected value due to exclusion data

In further study, Jezek et al [24] clarified the investigation is according to the presentation of vesicular and pustular fluid or scabs. It is two consecutive skin specimens within the first week and the third to the fourth week. In addition, serum specimen is also collected in case of fade of skin rash. Further, blood specimens were collected from vaccinated contacts who had a history of recent fever, conjunctivitis, lymphadenitis, or other doubtful clinical features. On the other hand, Jezek et al [24] clarified 14 people had positive serology tests without taking history which is against the criteria of collecting samples. However, the positivity may indicate vaccination rather than infection. Jezek et al [24] divided the contacts based on living and nonliving house and selected the secondary cases attack, which is 94% in both, which eliminate the contact reason. Therefore, the vaccine efficacy is 87.5% in total 56 secondary cases contacts. In the current study, several questions are raised of using the entire number of contacts based on the criteria of collecting sample to provide the attack rate leading to vaccine efficacy as well as the fourteen positive samples were collected which is against criteria. Further, the reason for selection of vaccinating secondary cases ignoring the primary cases is against the sample collection criteria in the first and third or fourth. The current study revises the 130 laboratory tests to provide the vaccine efficacy due to the restricted criteria of Jezek et al. [24] eliminating the rest contacts of vaccinated and unvaccinated cases which are free from contact historically and clinically. Jezek et al. [24] stated that the unvaccinated cases have 13.9 attack rate of younger than five years and 12.4% attack rate for younger than five years who is under 15 years. Based on the same data, the infection of unvaccinated household in different age younger than 15 are almost same beside the attack rate of older than 15 years is zero indicating insignificant of vaccination. Therefore, the laboratory investigation of cases must be accurate number to be in calculation of vaccine efficacy. The laboratory test for vaccinated and non-vaccinated samples are 110 and 449 is excluding the query of contact of both groups and including of the two-consecutive sample craters (primary and secondary cases). However, the fourteen positive cases unconsidered cases due to negative history or clinical features as well as the remaining contacts had considered missing data. Conversely, Jezek et al. [24] considered both which are against the selection sample criteria used in method. In current study, the household

Vaccine efficacy is calculated as the result of [(50/198) – (15/71)]/(50/198)}x100= [(0.2525252525252525-0.21126760563380280/ 0.2525252525252525] x100 whereas the total Vaccine efficacy is calculated as a result of [(74/449)–(18/110)]/ (74/449)} x 100 = [(0.1648106904231626 - 0.1636363636363636 /0.2837837837837838] x 100. Therefore, the household vaccine efficacy is 16.3% whereas total vaccine efficacy is 0.6%. The effectiveness of vaccine in Household is more accurate due to the same exposure risk whereas the total did not have the same risk for all cases.

However, the severity of clinical presentation in unvaccinated and vaccinated people found to be 74% and 39.5% [13]. This clear evidence of effective vaccine decreasing the incidence of severity of progress in development of acute respiratory distress syndrome, ronchopneumonia, pneumonitis, and encephalitis [13] in 24.5% compared to unvaccinated group. The severity of clinical presentation is variable may include consequences systematically such as respiratory system (acute respiratory distress syndrome, bronchopneumonia, pneumonitis), nervous system (Encephalitis, ocular infection e.g. keratitis and blindness), gastrointestinal system (diarrhea and vomiting reaching to dehydration) [13]. Kabuga and Zowalaty [25] estimate the monkeypox mortality rate between zero and ten percent whereas the World Health Organization estimates the monkeypox mortality rate between 3% and 6%. In current research study, the mortality rate ranges from 2.7 to 10.1% when it estimated mortality rate of confirmed cases of monkeypox is 4.4% globally (Table 1). Mortality is higher in children, young adults, and immunocompromised individuals based on the World Health Organization. The mortality rate can be decreases as the vaccine intake increases. Yearly, the incidence of rate of monkeypox is 63 persons per million in the Bumba [22] whereas it raises to 553 persons per million in Democratic Republic Congo [26] due to insufficient vaccination.

5. CONCLUSION

The validity of vaccine efficacy depends on several factors including the case definition which should be standardized and practical consistently as well as the vaccine date well identified, and infection exposure were equal in vaccinated and unvaccinated groups. Further, sex, age and race are other factors that may modified from area to other area that affect the

result of vaccine efficacy. Coexistence of conditions or diseases such as malnutrition or diabetes may also become other factors must considered clinically rather than statistically. Several preventive measures such as avoiding face-to-face exposure using personal protective equipment (Using mask, face shield, disposable gloves google. Etc.). The contact divided into direct physical contact such as sexual contact including multiple contact partners and condomless sexual contact or indirect contaminated materials such as clothing or bedding. Avoid gathering place and put triage point to infected cases and contacts across. Healthcare workers must adhere to precautions including hand hygiene and use personal protective equipment (PPE) such as gloves, face masks, gowns, and goggles. Further, suspected and confirmed cases should not donate blood, cells, tissue, organs, breast milk, or semen. Avoid traveling cross country and get smallpox vaccination. Scientists and clinicians reported any monkey case is also preventive measures to control an outbreak. Further breast-feeding should be discontinued preventing transmission from mother to child or the other way around. It is a clear message passing to entire scientist to find urgent monkeypox vaccine rather than depending on smallpox vaccine effectiveness. It alerts scientists and clinicians to prepare their self for endemic, epidemic, or pandemic disease may occur due to lacking effectiveness vaccine and treatment.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Reynolds MG, Yorita KL, Kuehnert MJ, et al. Clinical manifestations of human monkeypox influenced by route of infection. J Infect Dis. 2006;194:773.

2. Ladnyj ID, Ziegler P, Kima E. A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo. Bull. World Health Organ. 1972;46(5):593-597.

3. Edward Jenner. An enquiry into the causes and effects of the varriolae vaccinae; A disease discovered in some of the western counties of England, particularly Gloucestershire, and known by the name of the cowpox; 1798.

4. Multi-country monkeypox outbreak in non-endemic countries; 2022. Available:https://www.who.int/emergencies /disease-outbreak-news/item/2022-DON385 (Accesson 22 May 2022).

5. WHO. Second meeting of the international health regulations (2005) (IHR) Emergency committee regarding the multi-country outbreak of monkeypox; 2022.

6. Walker M. Monkeypox virus hosts and transmission routes: A systematic review of a zoonotic pathogen. biological sciences undergraduate honors theses; 2022. Available;https://scholarworks.uark.edu/bis cuht/69

7. Fine PE, Jezek Z, Grab B, Dixon H. The transmission potential of monkeypox virus in human populations. Int J Epidemiol. 1988;17(3)643-50.

8. Quiner CA, Moses C, Monroe BP, Nakazawa Y, Doty BJ, Hughes MC, McCollum MA, Ibata S, Malekani J, Okitolonda E, Carroll SD, Reynolds GM. Presumptive risk factors for monkeypox in rural communities in the Democratic Republic of the Congo. PLoS One. 2017;12(2):e0168664. DOI: 10.1371/journal.pone.0168664.

9. Antinori A, Mazzotta V, Vita S, Carletti F, Tacconi D, Lapini LE, D'Abramo A, Cicalini S, Lapa D, Pittalis S, Puro V, Rivano Capparuccia M, Giombini E, Gruber CEM, Garbuglia AR, Marani A, Vairo F, Girardi E, Vaia F, Nicastri E; INMI Monkeypox Group. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact. Italy, Euro Surveill. 2022;27:22. PMID: 35656836. DOI:10.2807/1560-7917.ES.2022.27.22.2200421.

10. Hammerschlag Y, MacLeod G, Papadakis G, Adan Sanchez A, Druce J, Taiaroa G, Savic I, Mumford J, Roberts J, Caly L, Friedman D, Williamson DA, Cheng AC,

McMahon JH. Monkeypox infection presenting as genital rash, Australia. Euro Surveill. 2022;27:2.
PMID: 35656835
DOI:10.2807/1560-7917.ES.2022.27.22.2200411

11. Perez Duque M, Ribeiro S, Martins JV, Casaca P, Leite PP, Tavares M, Mansinho K, Duque LM, Fernandes C, Cordeiro R, Borrego MJ, Pelerito A, de Carvalho IL, Núncio S, Manageiro V, Minetti C, Machado J, Haussig JM, Croci R, Spiteri G, Casal AS, Mendes D, Souto T, Pocinho S, Fernandes T, Firme A, Vasconcelos P, Freitas G. Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022. Euro Surveill. 2022;27:22. PMID: 35656830.
DOI:10.2807/15607917.ES.2022.27.22.2200424.

12. Vivancos R, Anderson C, Blomquist P, Balasegaram S, Bell A, Bishop L, Brown CS, Chow Y, Edeghere O, Florence I, Logan S, Manley P, Crowe W, McAuley A, Shankar AG, Mora-Peris B, Paranthaman K, Prochazka M, Ryan C, Simons D, Vipond R, Byers C. Watkins NA UKHSA monkeypox incident management team. Welfare W, Whittaker E, Dewsnap C, Wilson A, Young Y, Chand M, Riley S, Hopkins S. Monkeypox incident management team. community transmission of monkeypox in the United Kingdom, April to May 2022. Euro Surveill. 2022;27:22.
DOI:10.2807/1560-7917.ES.2022.27.22.2200422.
PMID:35656834.

13. Jezek Z, Szczeniowski M, Paluku KM, Mutombo M. Human monkeypox: Clinical features of 282 patients. J Infect Dis. 1987;156:293-8.

14. Di Giulio DB, Eckburg PB. Human monkeypox: An emerging zoonosis. Lancet Infect Dis. 2004;4:15-25.

15. Damon IK. Status of human monkeypox: Clinical disease, epidemiology, and research. Vaccine. 2011;29(4):D54–9.

16. Huhn GD, Bauer AM, Yorita K, et al. Clinical characteristics of human monkeypox, and risk factors for severe disease. Clin Infect Dis. 2005;41:1742.

17. Danet C, Fermon F. Management of a measles epidemic: Practical guide for doctors, nurses, laboratory technicians, medical auxiliaries and logisticians. Editor: Bachy C, Grouzard V. CHAPTER 7, Médecins Sans Frontières. Management of a measles epidemic. 2013 Edition.

18. World Health Organization. EB51/3 organisation mondiale de la santé executive board fifty-first session. Provisional agenda item 2. 2. Report on expert committee meetings. Report of the Director-General. 1972;1-25.

19. World health organization. (Zaire: Smallpox Cases by Month, 1968-1971) Epidemiological notes contained in this number: Surveillance-maintenance vaccination programmer Influenza, Smallpox Surveillance. List of Infected Areas. 1972;114.
Available:http://apps.who.int/iris/bitstream/handle/10665/218769/WER4710_109-113.PDF?sequence=1
Available:https://apps.who.int/iris/bitstream/handle/10665/146299/EB51_3_eng.pdf?sequence=1&isAllowed=y

20. Arita I, Jezek Z, Khodakevich L, Kalisa Ruti. Human monkeypox: A newly emerged ortbopox virus zoonotij in the tropical rain forestt of Africa. Am J Trop Hyg. 1985;34:781-9.

21. Jezek Z, Grab B, Szczeniowski MV, Paluku KM, Mutombo M. Human monkeypox: Secondary attack rates. Bull World Health Organ. 1988;66:465-70.

22. Dimon IK. Status of human monkeypox: Clinical disease, epidemiology, and research. Vaccine. 2011;29(4):D54-59.
DOI: 10.1016/j.vaccine. 2011.04.014

23. Jezek z, Marennikova SS, Mutumbo M, Nakano JH, Paluku KM, Szczeniowski. Human M. Monkeypox: A Study of 2,510 Contacts of 214 Patients. The Journal of Infectious Diseases. 1986;154(4):551-555.

24. Kabuga AI, El Zowalaty ME. A review of the monkeypox virus and a recent outbreak of skin rash disease in Nigeria. J Med Virol. 2019;91(4):533-540.

25. Rimoin AW, Mulembakani PM, Johnston SC, et al. Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo. Proc Natl Acad Sci U S A. 2010;107:16262–7.

26. World Health Organization-Regional Office for Africa (WHO/AFRO). Outbreaks and emergencies bulletin, Week:17. 2022;18. Brazzaville: WHO/AFRO; 2022.

Available:https://apps.who.int/iris/bitstream/handle/10665/354215/OEW19-0202052022.pdf

27. Nigeria Centre For Disease Control (NCDC). Monthly Update on Monkeypox (MPX) in Nigeria, Epi-week: 17. Jabi Abuja: NCDC; 2022.
Available:https://ncdc.gov.ng/themes/common/files/sitreps/ed4f642dd1b5b1f1adf277e1d48a98f8.pdf

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