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Original Article

Smallpox vaccination discontinuation and monkeypox incidence in an African endemic region: a reanalysis on the relationship between the withdrawal of smallpox vaccine and subsequent morbidity

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Abstract: Background: Monkey pox has expanded across Europe as a result of the widespread outbreak, creating a severe public health risk. Monkey pox is an uncommon pox infection that has reappeared due to zoonosis. Monkey pox has spread over Europe and North America, posing a serious public health risk. The regular smallpox vaccine has been shown to be effective against monkeypox. The suspension of smallpox immunization is currently being debated due to the possibility of a connection with the current monkeypox outbreak. In clinical immunology, the link between a desire for smallpox vaccination, low population immunity, and a higher incidence of monkeypox is an intriguing topic. Methods: This is a descriptive analysis done in the past. The writers investigate the situation in West Africa in this research. The available data on monkeypox incidence in an African endemic area was reassessed. Results: Based on a recent analysis of epidemiological data from an endemic area, there is no indication of a yearly ongoing increase in monkeypox incidence following the discontinuation of the smallpox vaccine, and incidence varies. Conclusion: There is no evidence of an annual increase in monkeypox incidence following the withdrawal of smallpox immunization.

Keywords: Monkeypox, small pox, vaccination

Introduction

New zoonotic pox diseases have evolved, in addition to the well-known pox infections, and they are now a global issue [1-13]. As a result of the broad outbreak, monkey pox has spread across Europe, posing a serious public health danger [2]. Monkey pox is a rare pox infection that has returned as a result of zoonosis [1]. Monkey pox has spread throughout Europe, creating a significant public health risk [2]. Monkey pox is an uncommon kind of pox that has resurfaced as a result of zoonotic activity. Human-to-human transfer is being researched at the moment [1]. The medical community is concerned as the number of reported cases in various nations climbs, and careful planning to coincide with a potential monkeypox outbreak is needed.

It has been demonstrated that the standard smallpox vaccine is effective against monkeypox. Attack rates in people with and without vaccination scars demonstrated that smallpox vaccination (which was phased out in 1980) gave approximately 85% protection against monkeypox [14]. The smallpox vaccine, however, has not been used frequently since 1970 due to global success in reducing the disease. The effect of seeking smallpox immunization on monkeypox epidemiology is a fascinating subject. It is projected that monkeypox virus will continue to be introduced into human populations from animal sources, and that the average volume and length of monkeypox epidemics will increase as vaccine-derived immunity in the population declines [15]. Monkeypox arose when the smallpox vaccine was unavailable for an extended period of time in West African

countries such as Nigeria and Congo. The relationship between a desire for smallpox vaccination, low population immunity, and a higher incidence of monkeypox is an intriguing topic in clinical immunology. In this paper, the authors examine the situation in West Africa.

Materials and methods

Study design

This is a retrospective study. A retrospective descriptive analysis of the available data was performed. A reappraisal of the available data on the incidence of monkeypox in an African endemic area was done. The inclusion is the specific data on epidemiological surveillance data in the African endemic area of monkeypox. A database search was initially conducted to get data for inclusion. PubMED (www.pubmed.com) was selected as the standard database. Search terms include "monkeypox", "incidence", and "Africa". Only legitimate published data found in PubMED, a global reference resource, was utilized. In the event that there is incomplete data, exclusion is performed. There were 209 publications found in the primary search (data as of July 2022). Only the publication with complete data on the incidence of monkeypox in endemic areas of Africa at different times after the suspension of smallpox immunization was chosen for further study.

The complete data can be found in a previous report that presented disease epidemiology over a 13-year period (between the 21st and 33rd years after smallpox vaccination discontinuation) [16]. The surveillance report lists 2,024 cases, all of them under 30 years of age, with an incidence rate ratio of 1.21 for men and women.

Statistical analysis

There is no comparison group because this is a descriptive study. The observed incidence rates from various time periods are compared. A descriptive statistical analysis was performed to analyze the distribution of appraised data. The distribution of the incidence over the studied period was assessed by a standard descriptive statistical analysis. Standard deviation, variance, skewness, and kurtosis were calculated. The main observation indicator is the distribution pattern or moments of a distribution of the incidence of monkeypox.

Regarding the observation indication, there are three important parameters, standard deviation, skewness, and kurtosis. The standard deviation measures the dispersion around the mean. In a normal distribution, at least 68 percent of cases lie within two standard deviations of the mean. Skewness is defined as a deviation or asymmetry from the symmetrical bell curve or normal distribution. Skewness should be close to zero for any symmetric data with a normal distribution. Negative skewness values indicate data that is slanted to the left, whereas positive skewness values indicate data that is slanted to the right.

Kurtosis denotes the degree of center peakedness or, alternatively, the fatness of the outlier. Positive kurtosis denotes a thin, pointed distribution, while negative kurtosis denotes a broad, flat distribution. Data is deemed normal if the skewness is between -2 and +2 and the kurtosis is between -7 and +7. An outlier is determined if kurtosis exceeds the normal range.

These three main parameters, known as the main observation indicators, are statistical parameters that describe data distribution. The standard deviation of a data distribution measures its spread. The greater the standard deviation of a data distribution, the more dispersed it is. Skewness is a measure of symmetry, or more specifically, the lack thereof. A symmetric distribution or data set is one that looks the same to the left and right of the center point. Kurtosis determines whether the data are heavy-tailed or light-tailed in comparison to a normal distribution. The pattern of monkeypox incidence distribution over time can be assessed using these three parameters in the current study. If the studied observation indicators show an abnormal distribution, it could indicate the presence of a disease epidemic, which could be seen in the analyzed time series data.

Results

Reappraised data

According to primary data, the observed incidence of monkeypox fluctuates over time (**Figure 1**). There is no specific direction of change in the incidence of monkeypox overtime during the study period (**Table 1**). The range of monkeypox incidence is between 0.64 to 3.11

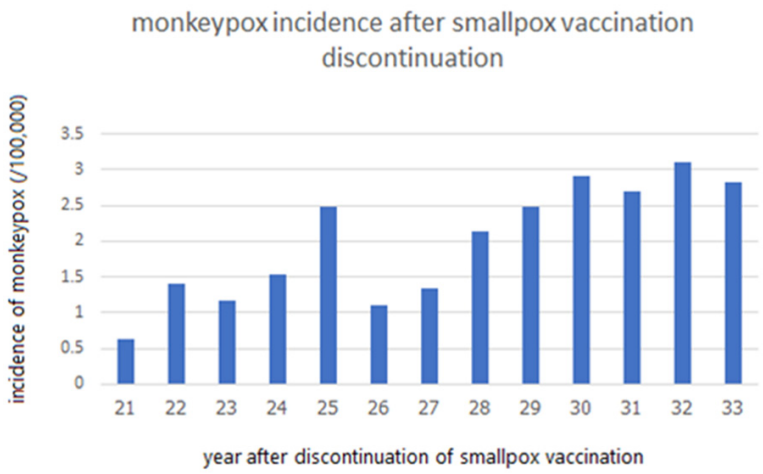

Figure 1. Observed incidence of monkeypox in this study.

cases/100,000 and the mean is 1.98 cases/100,000.

Observation indicator

The descriptive statistical analysis gave the standard deviation, skewness, and kurtosis equal to 0.62, -0.13, and 1.57, respectively. All three parameters for moments of a distribution test appear to be within normal limits. All the data lies within two standard deviations of the mean. Regarding skewness, the value falls within the range of -2 and +2. For kurtosis, the value falls in the range of -7 and +7. There is no outlier and the distribution is normal.

Discussion

A rare kind of pox called monkey pox has returned due to zoonotic disease. Research on human-to-human transmission is now underway [1]. As the number of cases recorded in various countries rises, the medical community is concerned, and cautious planning to coincide with a potential monkeypox outbreak is required [1-13]. Since it is known that the smallpox vaccine can contribute to the development of cross immunity to monkeypox, the effects of the phase-out of smallpox immunization are an intriguing topic. Prior to the advent of the smallpox vaccine, estimates of the general population's immunity ranged from 65.6 percent in 1970 to barely 2.2 percent (95 percent in 2018) in Africa, where monkeypox is an endemic disease. In 2016. 2.82/100,000 cases of probable monkeypox were reported in 2013, according to another study [16], up from 0.64/100,000 cases in 2001. According to estimates, more than 70% of the world's population is no longer immune to closely related orthopox viruses like monkeypox and smallpox due to cross-immunity. A new case of monkeypox is currently being reported [17]. In sub-Saharan Africa, monkeypox is prevalent in as-yet unidentified animal reservoirs, whereas its human epidemiology appears to be shifting [17-20].

Based on the current review of epidemiological data from an endemic area, there is no evidence of an annual increase in monkeypox incidence following the withdrawal of smallpox immunization. There is a variability in incidence. Nonetheless, the descriptive statistical analysis revealed no outliers and a normal distribution, indicating no local outbreak of the endemic disease. Based on the findings from the current statistical analysis on the observed incidence of monkeypox at different periods after smallpox vaccine discontinuation, there is a fluctuation in the pattern and there is no trend of increasing incidence as time passes. There is also no abnormal peak in the incidence of monkeypox overtime. It can be demonstrated that even more than 30 years after smallpox immunization was phased out in this area, there is still no emergent outbreak in this endemic zone. Outside of Africa, the current pandemic is occurring in Europe, America, and Asia [21, 22].

Although there has been a similar extended period of smallpox vaccination phase out in areas outside of Africa, there is still no explanation for the present outbreak. Basically, a smallpox vaccination can result in both a cross-immunity to monkeypox and immunity to smallpox [23]. Numerous medical researchers have hypothesized that a smallpox vaccination can lower immunity levels [17-20]. The diminished immunity against monkeypox is evident after decades of the routine smallpox vaccine being discontinued [16]. If the diminished cross-protective immunity from smallpox vaccination is a significant contributing cause to the current outbreak of monkeypox in 2022, then an increased incidence of monkeypox should be

Table 1. Reported incidence of monkeypox in an endemic area in Africa and period after discontinuation of smallpox vaccination

Period after smallpox vaccine discontinuation (year)	Morbidity rate (/100,000 local population)
21	0.64
22	1.4
23	1.16
24	1.53
25	2.48
26	1.11
27	1.33
28	2.13
29	2.48
30	2.91
31	2.69
32	3.11
33	2.82

seen over a longer period of time following the discontinuation of mass smallpox vaccination.

An important research question is on the possible interrelationship between the discontinuation of smallpox vaccination and the increasing incidence of monkeypox. A retrospective analysis of the available data on the incidence of monkeypox is necessary to analyze the trend. The assessment of the pattern of distribution of incidence of monkeypox incidence at different periods after the discontinuation of smallpox vaccination can give an explanation. The moment of distribution test, a widely used mathematical technique, is used by the authors of the current study to assess the incidence pattern of monkeypox in endemic parts of Africa in connection to times after the smallpox vaccination program was discontinued.

The study shows that the monkeypox incidence normally varies over time. No abnormal or excessive increase in the incidence of monkeypox is detected. Skewness analysis results can confirm the regular occurrence of the disease in the study area without the trend of increasing or decreasing, which is concordant with the nature of the endemic area of monkeypox in Africa. The kurtosis analysis result shows no outliers, confirming the absence of an epidemic in the study setting. Hence, there is no sign of an abnormal outbreak of monkeypox in the studied African setting. In fact, the current situation in 2022 is an abnormal outbreak of monkeypox outside Africa. The authors of the current report claim that there is no evidence of an increasing trend, and that the incidence of monkeypox in an endemic African setting is distributed normally. Therefore, it may not be conclusive that stopping smallpox immunization can cause a long-term increase in the incidence of monkeypox. This may not prove that the current monkeypox breakout problem is solely attributable to the end of the smallpox epidemic. Based on the authors' observation, there should be other factors apart from the discontinuation of smallpox vaccination that contributed to the current outbreak.

If fading immunity is the cause, it is problematic why the outbreak has only recently begun in some parts of the world and smallpox immunization has been discontinued for many years. The exact mode of transmission for the current outbreak is still unknown. The importance of sexual interaction may be emphasized while the involvement of other animal vectors in producing zoonotic or vector-borne disease transmission is currently being explored. According to the authors, it would be interesting to look into another aspect that may have contributed to the lower cross immunity against monkeypox caused by the suspension of widespread smallpox vaccination. The prospect of a mutant pathogen that has just developed and the effects of climate change that could cause an infection to emerge in a non-African environment are interesting factors that should be looked into. Isidro et al. discovered that whereas 2022 MPXV (lineage B.1) correlated with cases associated with an endemic nation in 2018-2019, it segregated into a distinct evolutionary branch, possibly showing continued fast evolution [24]. Considering climate factors, it has been established that the climate plays a key role in the transmission of MPX from wildlife to humans [25].

Conclusion

Based on the current review of epidemiological data from an endemic area, there is no evidence of an annual increase in monkeypox incidence following the withdrawal of smallpox immunization and there is a variability in incidence.

Disclosure of conflict of interest

None.

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