ORIGINAL ARTICLE ISSN (ONLINE): 3027-2998

JOHNSON ET AL. NEXUS OF MEDICINE AND LABORATORY SCIENCE JOURNAL

LEVELS OF C- REACTIVE PROTEIN IN PATIENTS DIAGNOSED WITH MONKEY POX IN OWERRI, IMO STATE, NIGERIA

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Received: 12th January, 2024
Accepted: 21st February, 2024
Published: 28th February, 2024
Available: https//www.nmlsj.org
Publisher: ScholarlyFeed

Cite as: Johnson SM, Ohiri JU. Levels of C-reactive protein in patients diagnosed with pox in Owerri, Imo State, Nigeria. Nexus Med Lab Sci J. 2024; 1(1):9-15

Abstract

Background: The human Monkey pox viral disease is an endemic zoonotic infection in some regions of Africa caused by monkey pox virus, with recent outbreaks occurring in several non-African countries

Aim: To determine the levels of C-reactive protein among Monkey pox patients attending Federal Medical Centre, Owerri, Imo State.

Methodology: The study was conducted at the Federal Medical Center Imo State. Participants were individuals seeking medical attention for various conditions. 28 Samples were collected between May 1 and 31, 2022, their samples were test for Monkeypox via Polymerase Chain Reaction assay at the molecular laboratory in Abuja, 14 came back positive. Dermatologic tests were also conducted.

Result: Predominantly aged 21-30, 57.1% male, and 42.9% students. Majority had symptoms for 1-10 days, identified as heterosexual, and unavailable pregnancy status. CRP concentrations were notably high. Acyclovir, antibiotics, and a combination of vitamins, anti-histamines, and zinc were common medications. Hospitalization in 85.7% cases, mostly lasting 1-10 days, with a positive treatment outcome for the majority, complications were observed in 21.4% of cases. Contact cases primarily occurred in the police cell and Corper's lodge

Conclusion: This study shows that the concentration of CRP suggested inflammatory response, therefore the reason for quick recovery within 1-10 days.

Keywords: *Hospitalization, Monkeypox, Polymerase Chain Reaction.*

INTRODUCTION

The human Monkeypox viral disease is an endemic zoonotic infection in some regions of Africa [1] caused by monkey pox virus, with recent outbreaks occurring in several non-African countries [2]. The cases reported in non-African countries were considerably few, until the year 2022, when the cases reported during outbreaks increased [1][3]. It is an orthopoxvirus.

There are several clinical manifestations characteristic of the infection. Typically, rash, fever and lymphadenopathy are the main clinical features of the disease condition [4][5]. The disease can range from mild to severe. Most cases of the disease presents with moderate clinical manifestations, requiring no hospitalization or treatment with antiviral drugs and agents. However, the severe form of the disease requires hospitalization and the use of anti-viral agents, owing to the associated complications [4][5][6]. The complications include; encephalitis, pneumonitis, secondary bacterial infections, keratitis, myocarditis, epiglottitis and deep tissue abscess.

Although there has been several outbreaks of Monkeypox virus epidemics globally, the most recent, is the outbreak of early May, 2022, which affected about 75 countries and resulted in 16,000 cases and 5 deaths, necessitating the World Health Organization (WHO) to declare it a Public Health Emergency of International Concern [7]. The cases of the disease, its spread and attendant mortalities vary across countries and regions of the world, as well as, the duration before containment of the disease and its spread.

In the 2022 outbreak of the disease, Portugal, for instance, recorded sustained human to human transmission of the virus, with 588 cases occurring within a space of three months, covering May to July, with the transmission of the infection suspected to occur through the sexual route [8][9].

Basic knowledge of the transmission of the virus is obtained from investigations conducted among infected populations in endemic regions of the world. Such investigations have revealed that its transmission is mainly through close contact with an infected individual [10]. Although animal to human transmission of the disease can occur, outbreak in the population is commonly associated with relatively poor hygiene measures among the endemic population [1]. The most recent outbreak of 2022 attests to this fact, especially, in non-endemic countries.

In the most recent outbreak of the disease in non-endemic regions of the world, there was difference in the affected population and clinical manifestation of symptoms, with the severity being minimal and the dominantly affected bod region being the ano-rectal region [11] and depicting transmission through men to men sexual intercourse [9]. However, the virus has also been detected in salivary and semen samples [12], thereby, eliminating the erroneous belief of solely sexual transmission.

Over the years, researchers had attempted to elucidate the actual clinical manifestations of Monkeypox disease, and as to whether the disease is actually asymptomatic, but could be transmitted in such physiological state or not [13]. To ascertain if asymptomatic cases are transmissible is crucial, as this will imply that identification of symptomatic cases alone is no longer sufficient to either diagnose the disease or contain its spread among a population.

C- reactive protein is an acute phase protein produced by the liver in response to certain conditions, such as infection. It is an inflammatory protein and is known to increase in its

concentration within the circulation due to the presence of infectious agents, such as the Monkeypox virus. The protein is pentameric in shape and its increase in plasma is occasioned by the secretion of interleukin- 6, which is released by macrophages and T-cells [14]. Although C- reactive protein plays a critical role in the determination of inflammatory reactions, a more effective measurement is the determination of highly sensitive C- reactive protein. It is both more sensitive and accurate in the determination of the exact concentrations of the protein in plasma concentration.

In a study conducted in Belgium by [15], it was reported that the Monkeypox virus can exist in asymptomatic carriers, who are also capable of transmitting the pathogen to other individuals through sex and other bod fluids. However, this is yet to be immunologically elucidated. This could lay to rest the perception that the virus can only be transmitted symptomatic individuals.

In the course of Monkepox disease, several proteins and other metabolites are observed to be altered, some of which are inflammatory proteins. To date, there is no known study regarding the levels of C-reactive proteins, an inflammatory protein, at least, within the study jurisdiction. This has necessitated this novel study, to determine the levels of C-reactive protein among Monkey pox patients in a tertiary hospital.

METHODOLOGY

The study was conducted at the Federal Medical Center, Owerri, Imo State. It is a tertiary health facility located in the heart of the capital, catering for numerous healthcare concerns of the populace, as well as, training of medical and allied medical personnel in diverse specialties. The facility operates both in-patient and outpatient services, with the Dermatology and Community Medicine clinics being part of it.

Ethical approval was given my the Ethics Committee of Federal Medical Centre, Owerri. To enrol for the study, participants provided signed written consent.

The participants of this study were individuals that routinely presented for other medical conditions, especially those involving the skin, as well as, fever and chills, sexually transmitted infections and oro-pharyngeal gonorrhea or chlamydia infections. Samples were collected and analyzed between May 1 and 31, 2022.

Polymerase chain reaction assay was conducted on 5ml of venous blood samples obtained from the patients in the molecular laboratory, immediately after collection, the samples were sent to the National Center for Disease Control [NCDC] in Abuja. Normal immunoassay steps were adhered to. The blood samples collected in Ethylene Di amine tetra acetic [EDTA] bottles were properly mixed with the anti-coaggulant in the bottle. This was employed to confirm the presence of the virus. Similarly, dermatologic tests were done on swabs obtained from the sites where necrotic tissues and inflammation were observed, while cellular debris was obtained by skin scrapings.

The swab sticks were placed back into their sterile containers and then into Ziplock bag, after proper labeling. All the collected samples were further placed in geo-styled pack with ice and transported to the laboratory for the analysis. Sample collection and analysis was done following strict compliance to the Infection Prevention and Control [IPC] guidelines, using sterile sample bottles, glove and personal protective equipment, keeping highest safety measures, due to the high infectivity of the virus. A total of 28 samples were taken, but only 14 came back positive for the virus.

Statistical analysis

The data from the study were presented in percentage to reflect the proportion of the groups of interest. Inferential statistics was not performed but the descriptive data were categorized based on already established cut-off values of C-reactive proteins.

RESULTS

Table 1. Socio-demographic characteristics (n= 14)

Variables	Frequency (n)	Percent (%)
Age (years)		
10-20	4	28.6
21-30	8	57.1
31-40	2	14.3
Gender		
Male	8	57.1
Female	6	42.9
Occupation		
Business	2	14.3
Student	6	42.9
Civil servant	2	14.3
Artisan	2	14.3
Housewife	1	7.1
Security	1	7.1

Majority of the patients were aged 21-30 years old, which is similar to the male gender dominance, 8(57.1%), while most of them were students, 6(42.9%) and the least was a housewife and security personnel, 1(7.1%) and the longest duration of the symptoms was 1-10 days, 9 (64.3%).

Table 2. General presentation/laboratory investigation of patients

Variables	Frequency (n)	Percent (%)
Duration of symptoms (days)		
1-10	9	64.3
11-20	2	14.3
21-30	3	21.4
Sexual orientation		
Heterosexual	13	92.9
Homosexual	1	7.1
Pregnancy status		
Not available	13	92.9
Present	1	7.1
CRP (0-10mg/L)		
11-20	12	85. 7
21-30	1	7.1
31 and above	1	7.1

The general presentation of the patients at the facility, as depicted in table 2 shows that 9(64.3%) had the longest duration of symptoms of 1-10 days, while the shortest duration of symptoms was among 2(14.3%) patients, with the most sexual orientation and pregnancy status being mostly heterosexual and not available respectively, 13(92.9%). The plasma C-reactive protein concentration was observed to be high and very high among all the patients.

Table 3. Medications Used

Variables	Frequency (n)	Percent (%)
Anti-viral agents		
Acyclovir	3	21.4
None	11	78.6
Antibiotics		
Yes	13	92.9
No	1	7.1
Other medications		
Vitamins, anti-histamines, zinc	4	28. 6
Vitamins, anti-histamines, zinc, loratidine	2	14.3

Vitamins, anti-histamines, zinc, loratidine, calamine lotion	3	21.4
Vitamins, zinc, seven keys	1	7.1
Vitamins, anti-histamines, zinc, loratidine, ibuprofen	4	28. 6

Table 3 above is the medication history of the patients which shows that 3(21.4%) used acyclovir anti-viral agent, 13(92.9%) used antibiotics and mostly 4(28. 6%) patients used vitamins, anti-histamines and zinc, while the least was 1(7.1%) patient that used vitamins, zinc and seven keys.

Table 4. Hospitalization history

Variables	Frequency (n)	Percent (%)
Hospitalization		
Yes	12	85.7
No	2	14.3
Reason for isolation		
Clinical	7	50.0
Clinical, isolation	7	50.0
Duration of hospitalization (days)		
1-10	6	42.8
11-20	4	28. 6
31 and above	4	28. 6
Outcome of treatment		
Alive	13	92.9
Dead	1	7.1
Time to resolution of rash		
None	2	18.2
Less than 10 days	5	45.5
10-20 days	4	36.4
Time to resolution of symptoms		
None	2	20.0
1-5 weeks	6	60.0
More than 5 weeks	2	20.0
Complications of treatment		
Yes	3	21.4
No	11	78.6
Type of complication		
None	11	78.6
Wound, infection, sepsis	3	21.4
Contact with case		
Yes	4	28. 6
No	10	71.4
Place of contact		
None	10	71.4
Police cell	2	14.3
Corper's lodge	2	14.3

Table 4 above shows that majority of the patients were hospitalized, 12(85.7%), with the reason for hospitalization being for isolation and clinical manifestations, 7(50.0%) each and the most duration of hospitalization was for 1-10 days, 6(42.9%), while the outcome of treatment was that almost all of them survived it, 13(92.9%). The time taken for the rash to resolve was mostly less than 10 days, 5(45.5%), the time for the symptoms to resolve was mostly 1-5 weeks, 6(60.0%), with complications in only 3(21.4%) patients and 10(71.4%) patients did not have contact with a case of the disease, but the few that did have contact with a case was at the Police cell and Corper's lodge, 2(14.3%) each.

DISCUSSION

C-reactive protein has been reported as an anti-inflammatory protein whose plasma concentration increases with presence of inflammatory conditions, such as in Monkeypox virus infection. This has been a similar finding in this study, in addition to highly sensitive C- reactive protein, which is observed as more sensitive than the former, when ascertaining the plasma concentration. The study investigated the level of C-reactive protein and some associated features in Monkeypox patients over a period of 30 days. The study premised on the fact that following the outbreak of the disease in May, 2020, the clinical features mimicked those of other commonly occurring diseases and in developing countries, there is a dearth of laboratory equipment required to effectively diagnose the disease, as well as, differentiate it from other commonly occurring or

related diseases. It was obvious in this study that C-reactive protein concentration was very high. This sets the pace for the strong suspicion of a viral infection, which upon further investigation was proven to be Monkeypox viral disease.

The patients presented at the tertiary health facility but suspected to have the disease, thus, their samples were collected and sent to the Central Reference Laboratory for further analysis and confirmation of the presence of the virus. The study was conducted devoid of gender, tribal or religious bias. Samples were collected and analyzed in strict compliance to international standards. Of all the suspected cases, for which samples were collected and analyzed, 14 came back positive. Those individuals were further investigated, leading to the results obtained.

Most of the respondents were between 21-30 years old, mostly males, 8(57.1%) and majorly students, 6(42.9%). This observation may not be unconnected with the sexually transmitted pathway of the viral agent causing the disease. This sexual route of transmission was also reported by [1], thereby, affirming the relevance of this study. The dominant age range observed in this study is acclaimed as upward, occasionally and adventurous, intermittently indulging in inappropriate amoral relationships, which can result in the transmission of the virus.

Individuals affected by the disease require hospitalization, which will necessitate effective diagnosis, treatment and monitoring of recovery, in addition to the associated complications [4] [5] [6]. However, the duration of symptoms and treatment varies, as well as, the agents employed for the management the condition. 9(64.3%) patients had the shortest duration of symptoms resolution of 1-10 days, while the most sexual orientation was heterosexual, 13(92.9%). The treatment of viruses usually takes long, but effective and appropriate treatment is expected to aid early resolution of symptoms. This could have accounted for the quick recovery of most patients. This observation is in agreement with the finding of [4] in their study of viruses, with special reference to Monkeypox.

This study observed that C-reactive protein was high among all the patients. Similar observation was reported by other authors in their study [8] [9]. This affirms that setting, age or location may not necessarily alter the CRP levels in patients with inflammation and especially Monkeypox virus. The medication history shows that 3(21.4%) patients used acyclovir anti-viral agent, 13(92.9%) used antibiotics and mostly 4(28. 6%) patients used vitamins, anti-histamines and zinc. Antibiotics have been reported as a mainstay for the treatment of complications associated with Monkeypox disease by [4] [5] [6], thus, being in consonance with the finding of this study, in which antibiotics was mainly.

Majority of the patients were hospitalized, 12(85.7%), with the most reason for hospitalization being for isolation and clinical manifestations, 7(50.0%) each and the most duration of hospitalization was for 1-10 days, 6(42.9%), while the most common outcome of the treatment was survival, 13(92.9%). Hospitalization of Monkeypox disease patients is a common and logical medical practice. This is associated with curbing the spread of the disease, as well as, ensuring the effective and controlled treatment of the patients. A similar study [12] also reported the importance of hospitalization in curbing the spread of the disease, thereby, affirming the findings of this study. The time taken for the rash to resolve was mostly less than 10 days, 5(45.5%), while time for symptoms to resolve was mostly 1-5 weeks, 6(60.0%), with complications in only 3(21.4%) patients and 10(71.4%) patients did not have contact with a case of the disease, but the few that did have contact with a case, was at the Police cell and Corper's lodge, 2(14.3%) each. Although this investigation revealed reduced contact with cases among the respondents, the sexual route may not have been taken into consideration, and is very crucial. A similar study by [15] confirmed and agreed with our study findings regarding resolution of rash and symptoms. In general, a study conducted in 2022 affirm that microbial infection could affect the level of biomechical parameters depending on the degree of the infection [16].

Conclusion

Monkeypox disease is a fatal, contagious medical condition prevalent in developing countries, but currently affecting some developed countries. Although a disease of public health importance, the required attention seems poor in developing countries. This stems from the poor awareness of the disease among the populace and rapid spread whenever there is an outbreak. Effective diagnostic equipment are required to achieve the desired results of preventing and curtailing the transmission, spread and management of the disease.

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