

D-DIMER LEVELS AND THE RISK OF THROMBO-EMBOLISM IN PATIENTS DIAGNOSED WITH MONKEYPOX VIRUS IN OWERRI, IMO STATE, NIGERIA

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Abstract

Background: D- dimer is a protein fragment formed when a blood clot is been dissolved in the body. It is associated with coagulation, which further play a role in the formation of thrombo-emboli.

Objective: To assess D-Dimer levels as a potential risk for thrombo-embolism in patients diagnosed with monkeypox virus

Methodology: The study which was conducted at Federal Medical Centre, Owerri, Imo State involved 23 participants presenting with various medical conditions, including skin issues and associated symptoms like fever, chills, and sexually transmitted infections. Samples collected between May 1 and 31, 2022, underwent immunoassay and dermatologic tests, adhering to strict infection prevention guidelines. Out of 23 samples, 14 tested positive for the virus, forming the basis for analysis and discussion.

Results: The examined socio-demographic characteristics and clinical presentations of 14 participants, with majority aged 21-30 (57.1%), male (57.1%), predominantly students (42.9%). Most experienced symptoms for 1-10 days (64.3%), and high D-dimer concentrations were noted in 92.9% of patients. Medication usage included antibiotics (92.9%) and various combinations of vitamins, anti-histamines, and zinc. Hospitalization was common (85.7%), primarily for 1-10 days, with a favorable treatment outcome (92.9%)

Conclusion: This study observed significant increase in the plasma concentration of D-dimer, which is dangerous due to its associated risk with thrombo-embolism.

Keywords: Hospitalization, Socio-demographic, Thrombo-embolism

INTRODUCTION

D-dimer is a protein fragment formed when a blood clot is dissolved in the body. It is associated with coagulation, which further play a role in the formation of thrombo-emboli. The molecule is usually undetectable, but can be detected at low levels. The presence of d-dimer is occasioned by the formation and breakdown of significant amounts of blood clots.

D-dimer is a global indicator coagulation activation and fibrinolysis, with its level measured in plasma by employing assays that are broadly used the diagnosis of acute venous thromboembolism [1][2]. It is considered a by-product of blood clot formation and breakdown of clot.

D-dimer is reported to be associated with the first time occurrence of future thrombosis [3]. In relation to venous thrombo-embolism, D-dimer poses a 2.5 times higher risk of its recurrence and its levels are observed to noticeably higher when oral anticoagulants are discontinued [4]. D-dimer is not only known to be associated with venous thromboembolism, in regards to coagulation. It is likely that the molecule also plays some roles of coagulation in other disease conditions, such as Monkeypox disease, and this may be fatal, if not properly diagnosed and managed. Some authours also posit that D-dimer is actively involved in the coagulation observed in COVID-19 patients [5]. Specifically, COVID- 19 is reported to be associated with hypercoagulability [5] and D-dimer is the molecule implicated as the aetiological agent.

The human Monkeypox, abbreviated as Mpox, is a viral disease, regarded as endemic zoonotic infection in some regions of Africa [6] caused by Monkey pox virus, with recent outbreaks occurring in several non-African countries [7]. The cases

reported in non-African countries were considerably few, until the year 2022, when the cases reported during outbreaks increased [6][8]. It is an orthopox virus. The disease condition is associated with complications, such as cardiac disease.

While D-dimer levels are known to be elevated in some disease condition, reflecting an inflammatory course, it could also be observed in non-disease conditions. [9] reports that elevated D-dimer can be found in presumably healthy individuals, but this should be indicative of an underlying disease condition.

D-dimer tests measure the amount of the molecule in blood, by ascertaining the presence of certain proteins, which rules out clotting disorders. A positive test suggests the presence of blood clot or blood clotting problems. The treatment is yet to be scientifically determined, however, antiviral agents are employed, with some measure of success.

The clinical manifestations are another area of concern, as it seems to resemble other clinical ailments of similar nature. Typically, there are lesions that are either firm or rubbery, of which the walls are well circumscribed, deep-seated, and clot-like in appearance, at the top of the lesion. Nucleic acid amplification tests, like the polymerase chain reaction are the main diagnostic tests, and exudates are obtained from crusts and swabs. Due to the fatality associated with the condition, it is important to determine some parameters associated with it, such as d-dimer. This is the basis for initiating this study.

Methodology

The study was conducted at the Federal Medical Center, Owerri, Imo State, 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 out-patient services, with the Dermatology and Community Medicine clinics being part of it.

Ethical approval was obtained from the Ethics Committee, Federal Medical Centre and a written consent signed by participants were obtained them before the were enrolled for the study.

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

Immunoassay was conducted on 5ml of venous blood samples obtained from the patients in the Molecular laboratory of the National Center for Disease Control [NCDC] in Abuja, immediately after collection. Normal immunoassay steps were adhered to. The blood samples collected in Ethylene Di amine tetra acetic [EDTA] bottles were

properly mixed with the anti-coagulant in the bottle. Similarly, dermatologic tests were done on swabs and skin crusts 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 in adherence to strict compliance of the Infection Prevention and Control [IPC] guidelines, using sterile sample bottles, hand gloves and personal protective equipment, keeping highest safety measures, due to the high infectivity of the virus. A total of 23 samples were taken, of which 14 came back positive for the virus and used for analysis and discussion of findings.

Statistical analysis

The data gathered from the study were presented in percentage to express the proportion of the group implicated. Also data were categorized into D-Dimer level based on established reference range.

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
D-DIMER (0.3-4.2miu/L)		
0-5	1	7.1
6-10	13	92.9

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 D-dimer concentration was high in most of the patients, 13(92.9%).

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, loratadine	2	14.3
Vitamins, anti-histamines, zinc, loratadine, calamine lotion	3	21.4
Vitamins, zinc, seven keys	1	7.1
Vitamins, anti-histamines, zinc, loratadine, ibuprofen	4	28.6

In table 3 above, the medication history 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. Social history

Variables	Frequency (n)	Percent (%)
Number of sexual partners		
None	2	14.3
1	9	64.3
2	1	7.1
More than 2	2	14.3
Travel history		
No	14	100.0
Animal contact		
No	14	100.0
Nature of animal		
No	14	100.0
Specimen for diagnosis		
Swab	1	7.1
Swab, blood	13	92.9
Other laboratory investigations		
Yes	11	78.6
No	3	21.4

The table above, table 4, shows that most of the patients had mostly 1(7.1%), sexual partner, 9(64.3%), with no travel history or animal contact, 14(100.0%), while swab and blood

specimens were mostly used, 13(92.9%) and other laboratory diagnosis were conducted for most patients, 11(78.6%).

Table 5. 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 5 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

D- dimer is a protein fragment commonly associated with the formation and breakdown of blood clot in the circulation. Its assay is important in diseases, such as Monkeypox disease, due to the cardiac complication, that can occasionally be fatal. This study investigated the level of D- dimer and some other associated features in Monkeypox patients over a period of 30 days. The study was premised on the fact that the clinical features of the disease mimicked those of other commonly occurring diseases and in developing countries,

there is scarcity of common 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 D- dimer concentration was very high, which sets the pace for a strong suspicion of a viral infection and confirmation of the disease.

The patients presented at the tertiary health facility and were suspected to have the disease. This necessitated the collection of their samples and sending same to the Central Reference Laboratory for further analysis and confirmation

or absence of the virus. The study accorded equal opportunity to gender, tribe and religion. The 14 samples that came back positive, led to the further investigation of the patients and the results obtained.

Majority of the respondents were aged between 21-30 years old, mostly males, 8(57.1%) and mostly students, 6(42.9%). This observation ascribed to the sexually transmitted pathway of the viral agent causing the disease. This sexual route of transmission was also reported by [6], which affirms the relevance of this study. The observed dominant age range in this study is acclaimed as upward and adventurous, intermittently indulging in inappropriate amoral relationships, which could result in the transmission of the virus.

The general presentation of the patients at the facility shows that 9(64.3%), being majority, had the longest duration of symptoms, 1-10 days, the most sexual orientation and pregnancy status was mostly heterosexual and no pregnancy respectively, 13(92.9%), while the plasma D-dimer concentration was high in most of the patients, 13(92.9%). Plasma D-dimer is not a commonly measured parameter, but it is important in cases of Monkeypox, due to the complications attributed to the parameter, such as the cardiac complications, that can become fatal. The findings of this study agree with that of [9], in regard to the increased concentration of D-dimer and its association with fatality. [6], and [8] also reported an increased duration of symptoms among the respondents in their study, thereby, affirming the legality of this study. This confirms that environment does not affect the peculiar symptoms of the disease. Rather, other host factors like age and genetic composition could be implicated.

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 [10], [11] and [12], thus, being in consonance with the finding of this study, in which antibiotics was mainly. Almost all the patients had mostly one sexual partner, 9(64.3%), with no travel history or animal contact in all of them, 14(100.0%), while swab and blood specimens were mostly used, 13(92.9%) and other laboratory diagnosis were conducted for majority patients, 11(78.6%). The sexual route remains a common pathway for the transmission of the virus causing the ailment, therefore, even one infected partner can transmit it to several persons [7]. Similarly, many infections of the sexual route are diagnosed employing swab and blood specimens, which could be the reason for the affirmed increased use of these specimens in our study, also observed by [7]. Most individuals affected by the Monkeypox disease require hospitalization, which will necessitate effective diagnosis, treatment and monitoring of recovery, in addition to the associated complications [10][11][12]. 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 [11] in their study of viruses, with special reference to Monkeypox. This also agree with the report by some authors who

reported the implication of microbial infection on changing biochemical parameters [13].

CONCLUSION

Monkeypox disease is both contagious and fatal, and the condition is prevalent in developing countries, but occasionally affects some developed countries. Poor hygiene could be a factor implicated in its transmission, however, the exchange of certain body fluids is reported. Effective diagnosis is important to properly manage the condition and D-dimer is one of the crucial parameters. 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. This study observed significant increase in the plasma concentration of D-dimer, which is dangerous due to the associated complications and consequent fatality.

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