



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Journal Pre-proof

The logo for the journal iLIVER, consisting of the word "iLIVER" in white, uppercase letters on a dark blue rectangular background.

Viral Diseases in Africa: Preventing the Outbreak of Acute Hepatitis of Unknown Etiology

Okereke Promise Udohchukwu, Innocent Kitandu Paul, Margareth Richard Mallya, Matilda K. Basinda, Sospeter Berling Sospeter, Juvenali Ruaichi

PII: S2772-9478(22)00069-X

DOI: <https://doi.org/10.1016/j.iliver.2022.10.002>

Reference: ILIVER 34

To appear in: *iLiver*

Received Date: 7 September 2022

Revised Date: 26 October 2022

Accepted Date: 28 October 2022

Please cite this article as: O.P. Udohchukwu, I.K. Paul, M.R. Mallya, M.K. Basinda, S.B. Sospeter, J. Ruaichi, Viral Diseases in Africa: Preventing the Outbreak of Acute Hepatitis of Unknown Etiology, *iLiver*, <https://doi.org/10.1016/j.iliver.2022.10.002>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2022 The Author(s). Published by Elsevier Ltd on behalf of Tsinghua University Press.

SHORT COMMUNICATION:**Viral Diseases in Africa: Preventing the Outbreak of Acute Hepatitis of Unknown Etiology****Okereke Promise Udohchukwu^{1,3*}, Innocent Kitandu Paul², Margareth Richard Mallya², Matilda K. Basinda², Sospeter Berling Sospeter², Juvenali Ruaichi².**

1. Faculty of Dentistry, College of Medicine, University of Nigeria
2. Catholic University of Health and Allied Science, Mwanza, Tanzania
3. YOHAN Research Institute

*Corresponding author: Okereke Promise Udohchukwu

Email: promise.okereke.240740@unn.edu.ng

ORCID ID: <https://orcid.org/0000-0002-6801-6207>

Keywords

Paediatric, Viral, Africa, Hepatitis, Unknown origin, Outbreak, Acute.

INTRODUCTION

Africa especially the sub-Saharan region has had an unfair share of outbreaks of viral disease. These include the ones that have threatened the global community such as SARS-CoV-2 and the ones endemic in the sub-region such as wild polio, Ebola and measles viruses. In a global community, outbreaks of new viruses and re-emergence of previously known ones are major concerns for the continent. This is particularly concerning considering the weak health system across the countries of Africa that can easily be overwhelmed by viral epidemics.

The first report of acute severe hepatitis of unknown etiology in children (ASHep UA) was made in Scotland, England on March 31, 2022. Since then, such cases have occurred in many countries or regions around the world, and the proportion of severe cases is relatively high, causing widespread concern. Since April 12, 2022, the European Center for Disease Control and Prevention (ECDC) and the official website of the World Health Organization (WHO) have published information about this disease for many times [1]. Subsequently, there was an outbreak of hepatitis of unknown origin among children, where nine pediatric patients in

Alabama, United States of America, tested negative for hepatitis viruses (A, B, C, D, E) and autoimmune conditions [2]. As a result, the World Health Organization (WHO) issued a warning about severe hepatitis of unknown origin among children [3]. Currently, over 1000 probable cases and 22 deaths due to severe acute hepatitis of unknown origin in pediatrics have been reported in 35 countries, mainly in WHO Regions of Europe, the Americas, Western Pacific Region, South-East Asia and Eastern Mediterranean [4]. It can progress to acute liver failure requiring liver transplant in some cases [5,6]. Africans have very limited capacity for liver transplant and preventive measures are both cost-effective and life saving for African children.

Whereas no cases have been reported in Africa, the uncertain etiology of acute hepatitis of unknown origin and globalization put African children at risk. Africa has a high pediatric population and is home to over 400 million children. It is therefore crucial to create an integrated early warning system in preventing severe acute hepatitis of unknown origin among African children.

EPIDEMIOLOGY

The United Kingdom reported 296 cases of acute hepatitis of unknown etiology among children under 10 years. [7], However, there have been 313 probable cases reported in other areas apart from the United Kingdom [8]. Globally, the number of probable cases has reached 1010 on 8 July 2022, while the United States contributes more than 296 cases [4,8]. Till date, there are no officially reported cases of acute hepatitis of unknown etiology in the African region. The weak health systems in Africa and attendant poor documentation across hospitals may be responsible for lack of official data.

ETIOLOGY

The exact etiology and pathogenesis of acute hepatitis of unknown origin affecting children is still under investigation. Nonetheless, laboratory investigations have ruled out common viral hepatitis (A, B, C, D, and E) as the cause in all reported cases [2,9]. However, many cases tested positive for Adenovirus subtype 41, making it the leading hypothesis. [5,9]. Moreover, identification of Adenovirus to the etiology comes with possible cofactors such as lack of prior exposure due to COVID-19 safety measures, co-infection with SARS-CoV-2 and other environmental factors [6].

EFFORTS AT CONTAINING THE OUTBREAK

Since the etiology of severe acute hepatitis is still unknown, there are no specific treatments. Public and clinical health incident responses in the affected regions have been activated to coordinate case finding with an investigation into the cause of illness in these children. More details about exposure histories, toxicology testing, and additional microbiological tests will be revealed by ongoing investigations by various national authorities. Additionally, a case-control study is underway in the United Kingdom to establish the frequency of adenovirus detection in the cases hospitalized with acute hepatitis compared to those hospitalized for other reasons. Furthermore, research actions are being coordinated across the WHO regions and partners to find the likely cause for this hepatitis of unknown origin.

WHO keeps sharing information with professional networks and specialists in liver units. In addition, WHO has developed guidance to ensure member states have adequate diagnostics, proper case investigation and reporting, as well as clinical characterization and management of acute liver failure in children [2].

PREVENTING AN OUTBREAK IN AFRICA

African countries are encouraged to identify, investigate and report any potential case fitting the acute hepatitis presentation. In addition, communities including families should be educated on the signs and symptoms of hepatitis, and the importance of seeking medical attention in time. Additionally, children presenting to health facilities with symptoms such as dark urine, jaundice and diarrhea should seek medical care and be kept in quarantine until all causes of hepatitis are ruled out. African medical practitioners should be educated and trained to be capable of identifying the disease at its earliest onset. Furthermore, multidisciplinary cooperation among pediatrics, emergency, infectious disease, gastroenterology, intensive care and laboratory should be emphasized. Diagnosis and treatment guidelines should be developed. The outbreak underscores the urgent need to strengthen health systems in the Africa region. Hospitals should be equipped with the capability to investigate and diagnose not only such viral hepatitis but many other emerging and re-emerging diseases threatening the continent. Families of African children should be able to promptly access health care without being further impoverished. A

universal and affordable health insurance is needed and out of pocket payments totally eliminated.

CONCLUSION

The outbreak of hepatitis of unknown origin among children is an urgent problem that should receive enough attention by clinicians, public health specialists, the community and health policy makers in Africa. Although the outbreak has not been reported in Africa, the continent should be ready to put in place measures necessary to tackle the disease should it occur. Strengthening the health system will go a long way in setting the standards required in tackling an outbreak of acute hepatitis and many other infectious diseases threatening the continent.

Funding

None.

Author contributions

Okereke Promise Udohchukwu: Conceptualization, manuscript writing and draft review; Innocent Kitandu Paul: Writing- Reviewing and Editing; Margareth Richard Mallya: Writing- Reviewing and Editing; Matilda K. Basinda: Writing- Reviewing and Editing; Sospeter Berling Sospeter: Writing- Reviewing and Editing; Juvenali Ruaichi: Writing- Reviewing and Editing.

Acknowledgements

We would love to appreciate Professor Agozie Ubesie for reviewing the final draft.

Declaration of conflict of interest

None.

Data available statement

Not applicable.

Ethics Statement

Not applicable.

Informed consent

Not applicable.

REFERENCES

1. Marsh K, Tayler R, Pollock L, Roy K, Lakha F, Ho A, Henderson D, Divala T, Currie S, Yirrell D, Lockhart M. Investigation into cases of hepatitis of unknown aetiology among young children, Scotland, 1 January 2022 to 12 April 2022. *Eurosurveillance*. 2022 Apr 14;27(15):2200318.
2. Baker JM, Buchfellner M, Britt W, Sanchez V, Potter JL, Ingram LA, et al. Acute hepatitis and adenovirus infection among children—Alabama, October 2021–February 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71:638–4
3. Organization. WHO: disease outbreak news; multi-country—acute, severe hepatitis of unknown origin in children. Available at: <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON376> (23 April 2022). Accessed 19 May 2022
4. World Health Organization. Severe acute hepatitis of unknown etiology in children - Multi-country. 2022. [Available at: <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON400>]
5. World Health Organization. Acute hepatitis of unknown aetiology. 2022. [Available at: <https://www.who.int/emergencies/emergency-events/item/2022-e000081>]
6. The Lancet Infectious Diseases. Explaining the unexplained hepatitis in children. 2022. DOI: [https://doi.org/10.1016/S1473-3099\(22\)00296-1](https://doi.org/10.1016/S1473-3099(22)00296-1)
7. Centers of Disease Control and Prevention (CDC). Interim Analysis of Acute Hepatitis of Unknown Etiology in Children Aged <10 Years — United States, October 2021–June 2022. [Retrieved from: <https://www.cdc.gov/mmwr/volumes/71/wr/mm7126e1.htm>]
8. ECDC. Epidemiological update issued 19 May 2022: hepatitis of unknown etiology in children. 2022. [Retrieved from: <https://www.ecdc.europa.eu/en/news-events/epidemiological-update-issued-19-may-2022-hepatitis-unknown-aetiology-children>]

9. ECDC. Update: Hepatitis of unknown origin in children. 2022. [Retrieved from: <https://www.ecdc.europa.eu/en/news-events/update-hepatitis-unknown-origin-children>]
10. ECDC. Increase in severe acute hepatitis cases of unknown etiology in children. 2022. [Retrieved from: <https://www.ecdc.europa.eu/en/increase-severe-acute-hepatitis-cases-unknown-aetiology-children>]
11. WHO. Acute hepatitis of unknown etiology in children - Multi-country.2022.[Retrieved from:<https://www.who.int/emergencies/disease-outbreak-news/item/DON-389>]