



Short Communication

Prospect of acute hepatitis E virus outbreak in the context of the COVID-19 Pandemic in Africa: A contingency plan

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ABSTRACT

Hepatitis E virus (HEV) is the primary cause of acute viral hepatitis in Sub-Saharan Africa (SSA). It is transmitted by oral-faecal route via contaminated water or animal products, which is more pronounced in SSA, where inadequate hygiene measures, low socioeconomic situation, and frail healthcare system increase HEV susceptibility. During the coronavirus disease-19 (COVID-19), numerous initiatives concerning viral hepatitis relief in SSA are implemented. However, national programs do not support most services and are neglected when national and local attention rests on the COVID-19 pandemic. Furthermore, during the COVID-19 pandemic, hepatitis E prevention and control programs were affected in low-income countries due to economic losses. Therefore, an interdisciplinary approach should be adopted to mitigate HEV infections during COVID-19.

1. Introduction

Sub-Saharan Africa (SSA) has the most reported infectious disease worldwide, leaving the area with a consequential burden in healthcare [1]. Among these infections, hepatitis E Virus (HEV) is of particular concern with approximately 15% of HEV cases worldwide and 29% of stillbirths in HEV-infected women, per SSA's report [2]. HEV, a primary cause of acute viral hepatitis in SSA [3], facilitates oral-faecal transmission by contaminated water or animal products [4]; this phenomenon is more pronounced in SSA, where inadequate hygiene measures, low socioeconomic status, and frail healthcare systems increase HEV susceptibility [1].

Although most HEV infections go unnoticed or present with mild symptoms, the mortality rate is between one to two percent in the general population. Infection is more dangerous among the immunocompromised sector, and pregnant women, where the risk of death may reach 25% [4] and fetuses may develop severe pathology [5]. HEV poses an enormous burden on its young population. This sector is most severely impacted by infection [2] due to SSA's high incidence of immunodeficient HIV patients [6], poor maternity and childcare [7], a high percentage of HEV outbreaks [8], and lack of infection control strategies [9].

The COVID-19 pandemic has negatively affected the surveillance and control of the hepatitis virus worldwide [31]. The lockdown resulted in reduced patient follow-up and evaluation, transfer of healthcare workers, and travel constraints that slowed down the diagnosis, resulting in late intervention and as a consequence, more complications and expense. Due to the coronavirus situation, only a few kids are receiving the hepatitis virus vaccination, this will disrupt the ongoing viral hepatitis eradication program and a high chance of achieving a hepatitis-free world may be lost [32].

On the other hand, despite the low number of Coronavirus disease-19 (COVID-19) cases in SSA relative to other world regions, the COVID-19 pandemic established an additional burden on the fragile healthcare system SSA [10]. At the same time, HEV outbreaks continued to be reported in various SSA countries [11]. In addition to hepatitis E, some African countries have faced other infectious diseases and viral outbreaks such as Lassa fever, HIV/AIDS, cholera, Dengue fever, Rift Valley fever, pneumonia and African Swine fever [12–19]. This article aims to determine the current situation, burden, and challenges facing HEV in Africa to limit future outbreaks.

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Table 1
Comparison between COVID-19 and hepatitis E virus.

	COVID-19	Hepatitis E
Similar symptoms	Fever, Nausea and vomiting, Fatigue [4,22]	
Unique symptoms	Loss of taste or smell, Congestion, Runny nose	Jaundice, Dark urine, Pale stools
Incubation period	2–14 days [26]	2–10 weeks [33]
Mortality Rate	2–7% [23]	1% (up to 20–25% in pregnant women in 3rd trimester) [4]
Way of transmission	Respiratory droplets	Oral-faecal route, contaminated waters

2. The situation of fighting hepatitis E virus before COVID-19 Pandemic in Africa

Hepatitis E is a leading cause of acute viral hepatitis worldwide, with an estimated 3.4 million symptomatic infections, over 44,000 deaths, and 3000 stillbirths every year [2]. Hepatitis E serves as an endemic in Africa with frequent outbreaks [9] and protracted outbreaks in East Africa in areas of civil conflicts and humanitarian emergencies [21]. Sanitation and access to potable water during endemics further exacerbate the fight against the infection and prevent adequate relief for populations already battling civil conflicts and humanitarian emergencies [21].

Moreover, HEV remains neglected with regard to public health awareness and funding [17]. As a result, the World Health Organization (WHO) launched a campaign in 2015 to eliminate viral hepatitis globally by 2030 [18]. In addition, in October 2016, Médecins Sans Frontières (MSF) organized a meeting to increase awareness around the burden of hepatitis E to propose a roadmap for encouraging broader interest in the disease and facilitating the use of an available efficacious vaccine [23].

Controlling hepatitis E is an evident challenge due to the limited supplies and the absence of an effective treatment¹. In fact, SSA has a shortage of data in about 50% of countries; outbreaks are more prone in refugees and displaced people; governments face difficulties finding the source of contamination, and inadequate awareness is limited to the general population and healthcare professionals [21].

3. Burden and current status of hepatitis E Virus in Africa during COVID-19 pandemic

During the spread of COVID-19, HEV served as a burden in countries with poor hygiene, where contaminated water is consumed. Hepatitis E outbreaks have been recorded in Asia, the Middle East, Africa, and Central America, affecting significant populations [24].

SSA faced three outbreaks of Hepatitis E amidst COVID-19 [20]. One of these outbreaks took place in Burkina Faso. According to the WHO, 442 cases of febrile jaundice were recorded between September 8 and November 24, 2020 [21]. The outbreak left 16 deaths, 15 of which were reported in pregnant and postpartum women [25].

The contrast in signs and symptoms between HEV and COVID-19 is evident, with HEV having several distinct symptoms that assist clinicians in distinguishing between a COVID-19 and HEV infection. The geographical distribution of HEV is also critical in determining the likelihood of infections (Table 1).

Although liver-related deaths in Covid-19 patients have been reported caused by elevated liver function tests attributed to the coronavirus disease and/or use of hepatotoxic drugs that may adversely affect patients, particularly those with underlying liver diseases [35], there are no direct reports on this aggravated onset of HEV in Covid19 patients, despite numerous studies for HAV, HBV, and HCV. Covid-19 co-infections are quite prevalent. COVID19 coinfections are relatively rare. Because the symptoms of COVID19 can be similar to those of many other

infectious illnesses, misdiagnosis or delayed diagnosis is unavoidable, and can have serious repercussions in certain situations [36]. As a result, it becomes crucial to mention any concurrent infectious illnesses linked with COVID19 infection in order to educate practitioners about the risks.

4. Current efforts and challenges Facing Responses to hepatitis E Virus in Africa during COVID-19 pandemic

The COVID-19 pandemic increases mortality, especially in low-income countries with limited resources [27,28]. The number of patients at hepatitis clinics dropped significantly during the pandemic in African countries, and a shortage of critical diagnostic tests was simultaneously at stake [29]. Numerous initiatives concerning viral hepatitis relief in SSA are implemented. Yet, national programs do not support most services and are neglected when national and local attention rests on the COVID-19 pandemic. However, some research has been conducted concerning Hepatitis E. The WHO has announced additional efforts to eliminate hepatitis by 2030 as the infection takes a heavy toll on lives and is considered a major public health burden. Access to safe food and water is a challenge but essential for the prevention and control of the hepatitis E epidemic [9]. The economic burden of the COVID-19 pandemic is a fresh challenge for countries, namely those in Africa, with limited resources.

5. Recommendations

Beyond the direct mortality and morbidity associated with COVID-19, the ongoing pandemic has taken a substantial toll on worldwide healthcare. The strain on combatting HEV has been disproportionately placed on resource-constrained regions [29,30].

Rigorous efforts are required to develop a sustainable program to mitigate the spread of HEV in SSA, where a significant proportion of hepatitis cases are found [21].

As primary healthcare centers have been in shortage or avoided by the public, there is a need to increase awareness among community members about the importance of approaching PHC centers for more focused community-based management. Moreover, the importance of prevention measures has been brought to the fore. There is a demand for awareness campaigns on the importance of good personal hygiene and general measures for food safety until an effective vaccine becomes widely accessible. Authorities are further recommended to ensure the availability of clean water supplies and proper disposal of faecal waste. Lessons can be learned from the benefits of large-scale COVID-19 surveillance, mass testing, and contact tracing, as similar strategies can be implemented with HEV. Although blood screening for HEV is costly, high-risk individuals (pregnant women and immunosuppressed persons) should be prioritized for such procedures [37,38].

The adoption of interdisciplinary initiatives is of utmost importance in mitigating the spread of HEV facilitated through the collaboration of healthcare experts and policymakers in the region. Irrespective of the negative impact of the Covid-19 pandemic on the eradication of the Hepatitis E virus, it is imperative that innovative and targeted strategies are integrated to preserve and develop low-income nations' health systems which will, in turn, lead to the elimination of the virus. This begins at the rural level, with the implementation of fundamental preventive care measures and the participation of international organizations and governments, as well as community support. The present epidemic paints a clear image of the healthcare system's issues and successes, allowing the world to improve and develop a comprehensive strategy. One of the most prevalent causes and high-risk factors for the development of liver cirrhosis, which is also a complication of viral hepatitis, is excessive alcohol abuse. The practice should be phased out, and public campaigns and education should be conducted. Psychological services and therapies should be disseminated to the general public in order to successfully reduce alcohol and drug consumption. It is impossible to overemphasize the importance of promoting a healthy lifestyle and

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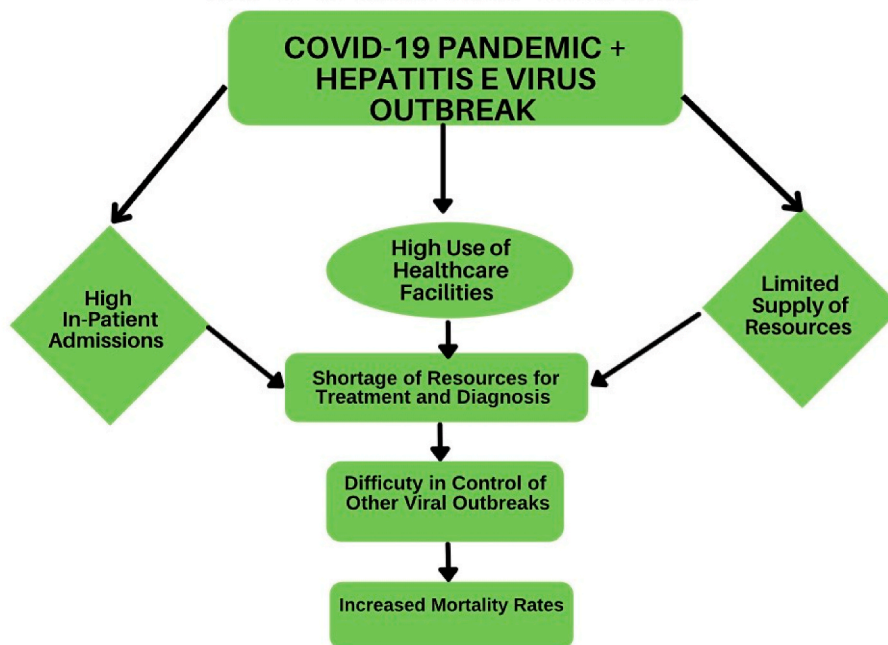


Fig. 1. Impact of Hepatitis E Virus outbreak amidst COVID-19 Pandemic in Africa.

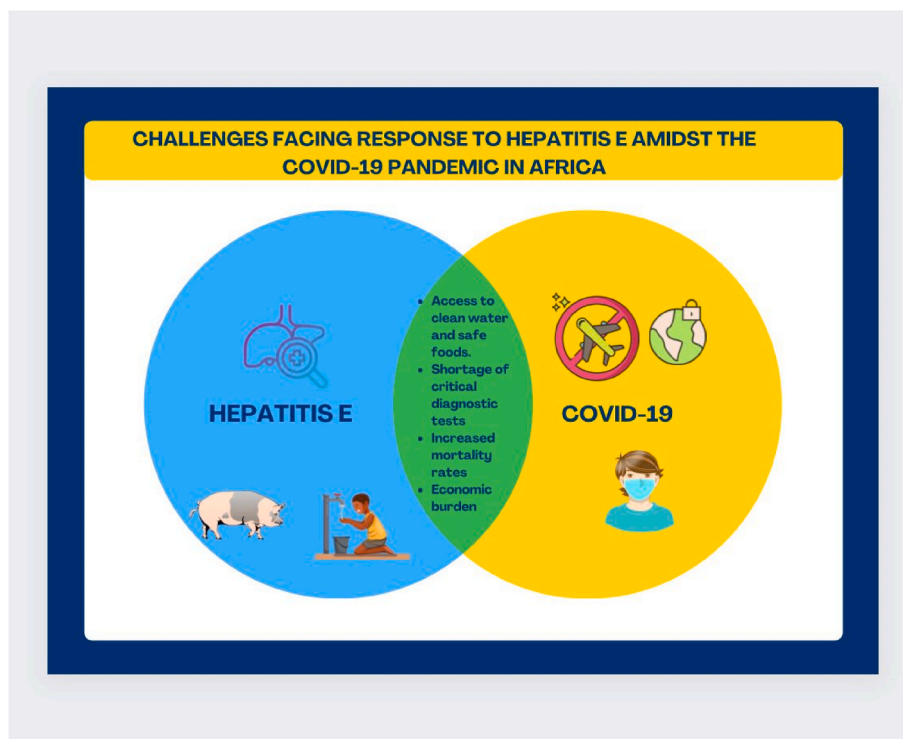


Fig. 2. A summary of challenges Facing Responses to Hepatitis E Virus in Africa during COVID-19 Pandemic.

keeping a healthy body weight to prevent obesity and preserve liver health, which includes avoiding the aforementioned causal risk. Antiviral therapy distribution to afflicted patients, as well as accessible and affordable access, with a focus on regimen compliance, is critical [34,37, 38].

6. Conclusions

Because of the COVID-19 pandemic, there is likely to be a lack of attention to preventing viral hepatitis. However, eradicating viral hepatitis in Africa would necessitate an innovative and targeted strategy to adopt novel ways to preserve and develop low-income nations' health

systems; this begins at the grassroots level, with the implementation of fundamental preventive care measures and the participation of international organizations and governments, as well as community support. In addition, the present pandemic paints a clear image of the healthcare system's issues and successes, allowing the country to improve and formulate a strategic plan.

Ethical approval

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Author contribution

Olivier Uwishema: Conceptualization, Project administration, Writing-review, and Designing, Manuscript writing: Oluyemisi Adekunbi; Olivier Uwishema; Irem Adanur and Helen Onyeaka, Olivier Uwishema: Reviewed and edited the first draft, Helen Onyeaka, PhD: Reviewed the final draft, Fig. 1 was drawn and analyzed by authors Oluyemisi Adekunbi^{1,4} and Olivier Uwishema^{1,2,3*}, Fig. 2 was drawn and analyzed by authors Oluyemisi Adekunbi^{1,4} and Olivier Uwishema^{1,2,3*}

Please state any conflicts of interest

No conflicts of interest declared.

Registration of research studies

1. Name of the registry: **Not Applicable**
2. Unique Identifying number or registration ID: **Not Applicable**
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Consent

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List of Abbreviations

HEV	Hepatitis E Virus
HIV	Human Immunodeficiency Virus
AIDS	Acquired Immunodeficiency Syndrome
COVID-19	Coronavirus Disease of 2019
SSA	Sub Saharan Africa
WHO	World Health Organization
MSF	Médecins Sans Frontières

References

- [1] F. Mboussou, P. Ndumbi, R. Ngom, et al., Infectious disease outbreaks in the African region: overview of events reported to the world health organization in 2018, *Epidemiol. Infect.* (2019) 147, <https://doi.org/10.1017/S095026881900191>.
- [2] D.B. Rein, G.A. Stevens, J. Theaker, J.S. Wittenborn, S.T. Wiersma, The global burden of hepatitis E virus genotypes 1 and 2 in 2005, *Hepatology* 55 (4) (2012) 988–997, <https://doi.org/10.1002/hep.25505>.
- [3] N. Kamar, R. Bendall, F. Legrand-Abbravanel, et al., Hepatitis E. *The Lancet*. 379 (9835) (2012) 2477–2488, [https://doi.org/10.1016/S0140-6736\(11\)61849-7](https://doi.org/10.1016/S0140-6736(11)61849-7).
- [4] World Health Organization, WHO. Hepatitis E. *Who.Int*, July 8, 2019. Published, <https://www.who.int/news-room/fact-sheets/detail/hepatitis-e>. (Accessed 19 July 2021).
- [5] L.J. Krain, A.B. Labrique, J.E. Atwell, K.E. Nelson, Fetal and neonatal health consequences of vertically transmitted hepatitis E virus infection, *Am. J. Trop. Med. Hyg.* 90 (2) (2014) 365–370, <https://doi.org/10.4269/ajtmh.13-0265>.
- [6] HIV/AIDS, Regional Office for Africa, WHO, 2018. Published, <https://www.afro.who.int/health-topics/hivaids>. (Accessed 19 July 2021).
- [7] Pearson L, Larsson M, Fauveau V, Standley J. *Childbirth Care*. World Health Organization: WHO Accessed July 19, 2021. https://www.who.int/pmnch/media/publications/aonsectionIII_3.pdf?ua=1.
- [8] A. Carratalà, S. Joost, Population density and water balance influence the global occurrence of hepatitis E epidemics, *Sci. Rep.* 9 (1) (2019), <https://doi.org/10.1038/s41598-019-46475-3>.
- [9] Causes of Death 2008: Data Sources and Methods, Department of Health Statistics and Informatics World Health Organization, Geneva, 2011. https://www.who.int/healthinfo/global_burden_disease/cod_2008_sources_methods.pdf. (Accessed 19 July 2021).
- [10] Africa Faces Looming Health Disaster as COVID-19 Cases Surge, Delta Variant Spreads - World. ReliefWeb, June 24, 2021. Published, <https://reliefweb.int/report/world/africa-faces-looming-health-disaster-covid-19-cases-surge-delta-variant-spreads>. (Accessed 19 July 2021).
- [11] Weekly Bulletin on Outbreaks and Other Emergencies, WHO, March 14, 2021. Published, <https://apps.who.int/iris/bitstream/handle/10665/340188/OEW11-0814032021.pdf>. (Accessed 19 July 2021).
- [12] O. Uwishema, B. Alshareif, M. Yousif, M. Omer, A. Sablay, R. Tariq, A. Zahabioun, R.M. Mwazighe, H. Onyeaka, Lassa fever amidst the COVID-19 pandemic in Africa: a rising concern, efforts, challenges, and future recommendations, *J. Med. Virol.* 93 (12) (2021) 6433–6436, <https://doi.org/10.1002/jmv.27219>.
- [13] O. Uwishema, C. Taylor, L. Lawal, N. Hamidah, I. Robert, A. Nasir, E. Chalhoub, J. Sun, B.T. Akin, I. Adanur, R.M. Mwazighe, H. Onyeaka, The syndemic burden of HIV/AIDS in Africa amidst the COVID-19 pandemic, *Immun., Inflamm. Dis.* 10 (1) (2022) 26–32, <https://doi.org/10.1002/iid3.544>.
- [14] O. Uwishema, G. Ayoub, R. Badri, H. Onyeaka, C. Berjaoui, E. Karabulut, H. Anis, C. Sammour, F. Mohammed Yagoub, E. Chalhoub, Neurological disorders in HIV: hope despite challenges, *Immun., Inflamm. Dis.* 10 (3) (2022), e591, <https://doi.org/10.1002/iid3.591>.
- [15] O. Uwishema, M. Okereke, H. Onyeaka, M.M. Hasan, D. Donatus, Z. Martin, L. A. Oluwatomisin, M. Mhanna, A.O. Olumide, J. Sun, I. Adanur, Threats and outbreaks of cholera in Africa amidst COVID-19 pandemic: a double burden on Africa's health systems, *Trop. Med. Health* 49 (1) (2021) 93, <https://doi.org/10.1186/s41182-021-00376-2>.
- [16] O. Uwishema, E.M. Nnagha, E. Chalhoub, G. Nchasi, R.M. Mwazighe, B.T. Akin, I. Adanur, H. Onyeaka, Dengue fever outbreak in Cook Island: a rising concern, efforts, challenges, and future recommendations, *J. Med. Virol.* 93 (11) (2021) 6073–6076, <https://doi.org/10.1002/jmv.27223>.
- [17] O. Uwishema, E. Chalhoub, T. Torbati, S.C. David, C. Khoury, L. Ribeiro, Y. Nasrallah, B.K. Bekele, H. Onyeaka, Rift Valley fever during the COVID-19 pandemic in Africa: a double burden for Africa's healthcare system, *Health Sci. J.* 5 (1) (2022), e468, <https://doi.org/10.1002/hsr2.468>.
- [18] O. Uwishema, H. Onyeaka, B.A.A. Alshareif, M.E.A. Omer, A.L.R. Sablay, R. Tariq, R.I.H. Mohamed, A. Zahabioun, M.Y.E. Yousif, E. Chalhoub, M.R. Tovani-Palone, Current context of pneumonia amidst the COVID-19 pandemic in Africa, *J. Contemp. Stud. Epidemiol. Public Health.* 2 (2) (2021), ep21007, <https://doi.org/10.30935/jconsep/11281>.
- [19] O. Uwishema, E. Chalhoub, A. Zahabioun, S.C. David, C. Khoury, T.H. Al-Sarairah, B.K. Bekele, R.M. Mwazighe, H. Onyeaka, The rising incidence of African swine fever during the COVID-19 pandemic in Africa: efforts, challenges and recommendations, *Int. J. Health Plann. Manag.* 37 (1) (2022) 561–567, <https://doi.org/10.1002/hpm.3357>.

- [20] M. Pérez-Gracia, M. García, B. Suay, M. Lindemann, Current knowledge on hepatitis E, *J. Clin. Trans. Hepatol.* 3 (2) (2015), <https://doi.org/10.14218/jcth.2015.00009>.
- [21] H. Bagulo, A.O. Majekodunmi, S.C. Welburn, Hepatitis E in sub saharan Africa – a significant emerging disease, *One Health* 11 (2020), 100186, <https://doi.org/10.1016/j.onehlt.2020.100186>.
- [22] Global Health Sector Strategy on Viral Hepatitis 2016-2021 towards Ending Viral Hepatitis, WHO, 2016. <http://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf?sequence=1>. (Accessed 20 July 2021).
- [23] The End of Viral Hepatitis by 2030 Is Impossible without Tackling Hepatitis E. Médecins Sans Frontières (MSF), December 9, 2016. Published, <https://www.msf.ch/nos-actualites/articles/end-viral-hepatitis-2030-impossible-without-tackling-hepatitis-e>. (Accessed 20 July 2021).
- [24] Hepatitis E Questions and Answers for Health Professionals | CDC, October 27, 2020. Published, www.cdc.gov. (Accessed 20 July 2021), <https://www.cdc.gov/hepatitis/hev/hevfaq.htm#section2>.
- [25] Acute Hepatitis E – Burkina Faso, November 27, 2020. Published, www.who.int. (Accessed 20 July 2021), <https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON300>.
- [26] Centers for Disease Control and Prevention, Coronavirus Disease 2019 (COVID-19) – Symptoms, Centers for Disease Control and Prevention, February 22, 2021. Published, <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>. (Accessed 20 July 2021).
- [27] Mortality Risk of COVID-19 - Statistics and Research, Our World in Data, 2021. Published, <https://ourworldindata.org/mortality-risk-covid>. (Accessed 21 July 2021).
- [28] T. Robertson, E.D. Carter, V.B. Chou, et al., Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study, *Lancet Global Health* 8 (7) (2020) e901–e908, [https://doi.org/10.1016/s2214-109x\(20\)30229-1](https://doi.org/10.1016/s2214-109x(20)30229-1).
- [29] M. Lemoine, J.U. Kim, G. Ndow, et al., Effect of the COVID-19 pandemic on viral hepatitis services in sub-Saharan Africa, *Lancet. Gastroenterol. Hepatol.* 5 (11) (2020) 966–967, [https://doi.org/10.1016/s2468-1253\(20\)30305-8](https://doi.org/10.1016/s2468-1253(20)30305-8).
- [30] O. Uwishema, E.E. Elebesunu, O. Bouaddi, A. Kapoor, S. Akhtar, E. Fortune, A. Chaudhary, H. Onyeaka, Poliomyelitis amidst the COVID-19 Pandemic in Africa: Efforts, Challenges and Recommendations, *Clinical Epidemiology and Global Health*, 2022, <https://doi.org/10.1016/j.cegh.2022.101073>.
- [31] C. Wingrove, L. Ferrier, C. James, S. Wang, The impact of COVID-19 on hepatitis elimination, *Lancet. Gastroenterol. Hepatol.* 5 (9) (2020) 792–794.
- [32] H. Karimi-Sari, M.S. Rezaee-Zavareh, COVID-19 and viral hepatitis elimination programs: are we stepping backward? *Liver Int.* 40 (8) (2020), 2042–2042.
- [33] World Health Organization, Hepatitis E, Retrieved from, <https://www.who.int/news-room/fact-sheets/detail/hepatitis-e>, 2022, June, 02.
- [34] J. Sun, O. Uwishema, H. Kassem, M. Abbass, L. Uweis, A. Rai, R. El Saleh, I. Adanur, H. Onyeaka, Ebola virus outbreak returns to the Democratic Republic of Congo: an urgent rising concern, *Ann. Med. Surg.* (2022), <https://doi.org/10.1016/j.amsu.2022.103958>.
- [35] S.A. Alqahtani, M. Buti, COVID-19 and hepatitis B infection, *Antivir. Ther.* 25 (8) (2020) 389–397.
- [36] H. Eshaghi, V. Ziaee, M. Khodabande, M. Safavi, E. Haji Esmail Memar, Clinical Misdiagnosis of COVID-19 Infection with Confusing Clinical Course, *Case Reports in Infectious Diseases*, 2021, 2021.
- [37] O. Uwishema, R. Badri, H. Onyeaka, M. Okereke, S. Akhtar, M. Mhanna, B. Zafar, A. Zahabioun, K.A. Said, M.R. Tovani-Palone, Fighting Tuberculosis in Africa: the Current Situation amidst the COVID-19 Pandemic. *Disaster Medicine and Public Health Preparedness*, vols. 1–12, Advance online publication, 2022, <https://doi.org/10.1017/dmp.2022.142>.
- [38] L. Greene, O. Uwishema, A. Nicholas, A. Kapoor, C. Berjaoui, E. Adamolekun, C. Khoury, F. Mohammed, H. Onyeaka, Crimean-Congo haemorrhagic fever during the COVID-19 pandemic in Africa: efforts, recommendations and challenges at hand, *Afr. J. Emerg. Med. : Revue africaine de la medecine d'urgence* 12 (2) (2022) 117–120, <https://doi.org/10.1016/j.afjem.2022.02.004>.