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ENHANCING THE MANAGEMENT OF SEVERE LASSA FEVER IN THE SUB-REGION

Lassa fever (LF) was first reported formally from Nigeria in 1969. Characterized by recurrent annual outbreaks in the dry season, it is endemic in many West African countries, principally Nigeria, Sierra Leone, Liberia, and Guinea.[1] Arising from the high incidence of morbidity and mortality associated with the outbreaks, it is of great medical and public health importance. About 20% of the patients have severe infections, which carries a high case fatality rate, previously >50% among hospitalized patients during outbreaks but currently under 20% in some referral centers.[2]

In this edition of the Journal, Onuh and Uloko report a case of severe LF with favorable outcome thought to be due to early diagnosis and treatment. The claim is debatable if rigorous criteria are applied: the patient was within both the favorable age bracket of 15-50 years[3] and favorable time from onset of illness of ⩽ 6 days.[4] He had only abnormal bleeding among the 4 generally acclaimed clinical indices of severe LF.[2] In the absence of respiratory failure, coagulopathy, acute kidney injury, septic shock, hyperbilirubinemia or encephalopathy, he had a seemingly highly favorable sequential organ failure assessment (SOFA) score;[5,6] and he has no infectious co-morbidity, while the only indicator of a severe infection was hepatic a transaminase level >150 iu/l.[4] Still, the claim that early diagnosis and treatment is of importance to the outcome could stand.

The report raises at least 2 other issues, however. ***First***, the impact of early diagnosis and treatment on outcome has been known for well over 3 decades.[4] What then has militated against the practice in the sub-region? The factors might not be far fetched: a low clinical index of suspicion among physicians, whereas a high index is essential to the diagnosis;[7] poor availability of confirmatory tests;[1,2,8,9] and the erstwhile frequent non-availability/affordability of ribavirin[8] are some. These are some of the reasons why the attending physicians to the index case should be commended, while acknowledging that the major factor that had sustained the poor practices was the erstwhile low political will of sub-regional governments to address the challenge of LF through sustained provision of the resources needed for diagnosis and surveillance, and appropriate clinical care.[1,8,10]

Second, had the index patient been more ill, could he have had ready access to enhanced care, which is key to improved outcome in severe LF/other severe viral hemorrhagic fevers (VHFs)?[2,11-13] Perhaps there might be more nays than ayes in answer to this question. The provision of enhanced/critical care is the way to go in the 'modern' treatment of severe LF,[14] and its dearth in most developing countries helps largely to explain the wide difference in outcome of severe VHFs in developed versus developing countries.[2,13] Its increasing availability over the years has steadily reduced the case fatality (CF) among hospitalized patients at Irrua Specialist Teaching Hospital, Nigeria, from well over 50% to fewer than 15-20% in recent times.[2] While it could be that other factors are also at play in the reduction, we strongly believe that the provision of enhanced care is a major one.[2]

The current approach to the management of confirmed LF rests on 5 prongs: [1] triage to determine the severity of illness. The presence of either septic shock, encephalopathy, acute kidney injury (AKI), and abnormal bleeding, particularly the former three,[2] or a SOFA/pSOFA score >8[5] is associated with an increased risk of death among all demographic groups of patients with LF.[2] Therefore, severely ill patients and those with co-morbidities should be referred to VHF designated referral centers; [2] provision of enhanced and/or critical care for severely patients;[2,15,16] [3] provision of antiviral therapy with ribavirin,[2,3,4] although it use in non-severely ill patients has questioned.[17] Other drugs such as favipiravir are being considered for use, either alone or in combination with ribavirin.[18] Favorable response has also sometimes been reported with the use of transfusion with convalescent blood or plasma, and with exchange blood transfusion but there is insufficient evidence to back these practices; and [4] assurance of the safety of healthcare workers (HCWs)[19] and prevention of nosocomial spread of infection through the appropriate use of personal protective equipment (PPE), pre- and post-exposure prophylaxis, and strict adherence to infection prevention and control (IPC) measures.[2,19,20] Treatment with antimalarial and antibiotic drugs should not be routine.

Enhanced and critical care revolves around 3 interrelated activities:[13,21] [1] the adequate monitoring of clinical-laboratory parameters for the early diagnosis of organ dysfunction,[5,6,] and monitoring of response to treatment; [2] institution of resuscitative management for the prevention of organ dysfunction; and [3] early provision of organ support where there is already established dysfunction. Both Ippollitto et al[15] and Hellman[16] have reviewed the necessity for, pathophysiologic basis of enhanced/critical care in the management of severe VHFs. The same principles and practice as in the treatment of severe sepsis/septic shock[5,15,16,22] are applicable in these regards. In the minimum,[13,21] it requires the availability of expertise and facilities

for the provision of cardiovascular support (including fluid resuscitation, and use of inotropic agents), respiratory support (provision of assisted ventilation for those with respiratory failure), renal support (provision of renal replacement therapy for those with severe AKI), neurologic support (reduction of increased intracranial pressure, and control of convulsions, including treatment of status epilepticus) and hematologic support (transfusion of blood and blood components).

An urgent issue is the state of our preparedness for provision of this life saving service as and where needed: how many institutions have established diagnostic capacity that is not dependent on overseas support for establishment and maintenance? How many have the capacity for adequate monitoring of severely ill patients? How many have the capacity for enhanced care, not to mention critical care in the provision of organ support? How much continuing professional education and/or development do HCWs involved in the care of these patients have to assure the capacity for use of the necessary facilities where available? And, how much protective gear, et cetera, is even made available to the HCWs? It might certainly not be practical to preposition the requirements in every area where LF is endemic, owing to the significant investments needed. However, the development of referral systems with suitably equipped and staffed apex centers that have the capacity for provision of the full range of critical care should be a given imperative in the sub region. The centers should be strategically located.

The establishment of these centers of excellence is supported by the WHO, and the Institute of Lassa Fever Research and Control, Irrua Specialist Teaching Hospital, Nigeria is in that mold.[2] There is also the Lassa Fever Center at Kenema General Hospital in Sierra Leone, and there is a growing effort in Nigeria to develop more centers. This trend should be encouraged, even as a similar effort is recommended for adoption by other national and subnational governments in the sub-region, particularly those countries that have a large/and or growing burden of LF. In addition, adequate surveillance and diagnostic capabilities to assure early diagnosis should be put in place, and our governments should heed the repeated calls to these needs,[1,2,8,23,24] and rise to the challenge of LF in the sub-region. We have remained a laughing stock because we seem incapable of defining our priorities, but the lessons and opportunities in the recent Ebola outbreaks as well as in the COVID-19 pandemic could be built upon to address the obvious needs. Lassa fever and other severe VHFs are no respecter of persons.

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