Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 161-162
DOI: 10.4415/ANN_24_03_01

COMMENTARY
"Undiagnosed" severe disease pseudo-outbreaks in Sub-Saharan Africa: a paradigm of syndemic events

Giovanni Rezza[1] and Marco de Feo[2,3]

[1]*Facoltà di Medicina e Chirurgia, Università Vita-Salute San Raffaele, Milan, Italy*
[2]*Laboratorio di Oncologia Molecolare, Istituto Dermopatico dell'Immacolata, IDI-IRCCS, Rome, Italy*
[3]*Saint Mary's Hospital Lacor, Gulu, Uganda*

Abstract
Several outbreaks of undiagnosed severe disease occurred in the Democratic Republic of Congo over the last year. Although this is not completely unusual, at least one of them raised an international concern until the determinants of the excess death were identified. Far from representing a real threat for people living in wealthy countries, most of these events are context related, and mainly due to a combination of poverty-related conditions, such as malnutrition, historic plagues like malaria, and vulnerability to common respiratory infections. Even though these syndemic events remain usually restricted to well defined geographical areas affected by poor resources, they merit attention since they represent an opportunity to improve health conditions in remote areas and a challenge to strengthen global preparedness against pandemic events.

Key words
- global health
- pandemics
- syndemic events
- tropical diseases
- preparedness

The occurrence of a high number of cases of a severe respiratory disease in the health zone of Panzi, Kwango province of Democratic Republic of Congo (DRC) at the end of last year, raised concern at international level. On December 8, 2024, the World Health Organization released a "Disease Outbreak News" reporting 406 cases with 31 deaths occurred between October 24 and December 5 of an undiagnosed disease characterized by fever, headache, cough, runny nose, and body aches; all severe cases were malnourished, the majority of them children, particularly under 5 years old [1]. The number of cases increased to 891 with 48 deaths (case-fatality rate: 5.4%) by December 16. Difficulty in breathing, anaemia, and severe malnutrition were associated with death. Although an increase in the number of cases is not considered to be unusual at the start of the rainy season, the observed number of deaths was higher than expected. This finding triggered the alert, which was amplified by the possibility that the outbreak might be due to an unknown – newly introduced – pathogen. However, laboratory results showed high levels of positivity to malaria and to common respiratory viruses, in particular influenza A (H1N1, pdm 09) and, to a lesser extent, rhinoviruses and SARS-CoV-2 [2].

The area affected by the "outbreak" was rural and remote, being sited at least 700 km (about 48 hours by road) away from Kinshasa. Although laboratory findings, showing the presence of common pathogens, were reassuring for the rest of the world, this event should not be neglected only because restricted to a context characterized by poor resources, low vaccine coverage, and difficult access to health services.

Actually, the Panzi event fits the classical criteria of a "syndemic", a term firstly used by Singer in the mid-90s and then applied to the COVID-19 synergistic global epidemic [3, 4]. A syndemic occurs when two or more diseases or health conditions cluster and interact within a population because of social and structural factors and inequities, leading to an excess burden of disease and/or mortality, and continuing health disparities [5]. The term "syndemic" perfectly applies to the Panzi "outbreak", where the excess mortality was due to the co-circulation of common respiratory viruses, in presence of severe malaria, and in the context of severe malnutrition.

On February 2025, a similar event occurred in the Equateur Province of DRC, with 53 deaths reported in Basankusu Health Zone, following a small cluster of 8 deaths occurred in the Balomba Health Zone in

Address for correspondence: Giovanni Rezza, Facoltà di Medicina, Università Vita-Salute San Raffaele, Via Olgettina 60, 20132 Milan, Italy. E-mail: rezza.giovanni@hsr.it.

January [6]. However, the excess death number rapidly decreased, and preliminary findings suggested the co-occurrence of several febrile illnesses in a hyperendemic area for malaria. Thus, also this event may be considered a pseudo-outbreak related to a context with underlying predisposing conditions due to the presence of high number of vulnerable individuals affected by common ailments of different nature.

The evidence that underlying conditions and poor-resource context play an important role in determining the occurrence of unusual clinical conditions which may be considered context-specific comes from the observation, once again in central African countries, of a high incidence of fibro-osseous odontogenic tumors, which are found exclusively in rural populations. These communities are characterized by cyclical nutritional deficiencies, environmental climate changes, extreme poverty, and malnutrition. They are often forced to rely on small wild animals, such as rats and bats, for food, and to drink water contaminated with the feces and urine of the same animals. This might increase the risk of infection with Lassa-like arenaviruses, that are commonly detected in odontogenic tumor specimens from children living in some remote areas of central Africa, and might be involved in their pathogenesis [7, 8].

Far for representing real pandemic threats or real menaces for people living in industrialized countries, the pseudo-outbreaks occurred in Panzi and in the Equateur Province of RDC, as well as other geographically restricted clinical entities, should not be downgraded to trivial local events. In fact, high population vulnerability and difficult access to diagnosis and care could affect the response to epidemic events. For this reason, they should be considered paradigmatic global health problems which necessitate adequate response. Although funding restrictions are currently affecting international organizations, financial and human resources to be mobilized in order to fit sustainable development goals in remote areas located in poor resources countries.

Conflict of interest statement

The Authors declare that there are no conflicts of interest.

Received on 7 June 2025.
Accepted on 7 July 2025.

REFERENCES

1. World Health Organization. Undiagnosed disease - Democratic Republic of the Congo. Disease Outbreak News. WHO; 2024. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON546.
2. World Health Organization. Acute respiratory infections complicated by malaria (previously undiagnosed disease) - Democratic Republic of the Congo. Disease Outbreak News. WHO; 2024. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON547.
3. Singer M, Bulled N, Ostrach B, Mendenhall E. Syndemics and the biosocial cnception of health. Lancet. 2017; 389(10072):941-50. doi: 10.1016/S0140-6736(17)30003-X
4. Horton R. Offline: COVID-19 is not a pandemic. Lancet. 2020;396(10255):874. doi: 10.1016/S0140-6736(20)32000-6
5. US Department of Health and Human Services. HIV.gov. Blog. Available from: https://www.hiv.gov.
6. World Health Organization. Cluster of community deaths in Basankusu. Equateur-Democratic Republic of the Congo. Disease Oubreak News. WHO; 2025. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2025-DON557.
7. de Feo M, De Leo C, Romeo U, Muti P, Blandino G, Di Agostino S. Arenavirus as a poten-tial etiological agent of odontogenic tumours in humans. J Exp Clin Cancer Res. 2020;39(1):34. doi: 10.1186/s13046-020-1540-1
8. de Feo M, Dilu Tamba F, Makaka Mutondo A, Kashitu Mujinga G, Odong OS, Castellani C, Pavesi L, Mpingabo PI, Ahuka-Mundeke S, Di Agostino S. Detection of the Lassa virus in a group of odontogenic bone tumor tissues. Anatomia. 2024;3(2):57-67. doi: 10.3390/anatomia3020006