Clinical features of patients isolated for suspected Ebola virus disease at Connaught Hospital, Freetown, Sierra Leone: a retrospective cohort study

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Summary

Background The size of the west African Ebola virus disease outbreak led to the urgent establishment of Ebola holding unit facilities for isolation and diagnostic testing of patients with suspected Ebola virus disease. Following the onset of the outbreak in Sierra Leone, patients presenting to Connaught Hospital in Freetown were screened for suspected Ebola virus disease on arrival and, if necessary, were admitted to the on-site Ebola holding unit. Since demand for beds in this unit greatly exceeded capacity, we aimed to improve the selection of patients with suspected Ebola virus disease for admission by identifying presenting clinical characteristics that were predictive of a confirmed diagnosis.

Methods In this retrospective cohort study, we recorded the presenting clinical characteristics of suspected Ebola virus disease cases admitted to Connaught Hospital's Ebola holding unit. Patients were subsequently classified as confirmed Ebola virus disease cases or non-cases according to the result of Ebola virus reverse-transcriptase PCR (EBOV RT-PCR) testing. The sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio of every clinical characteristic were calculated, to estimate the diagnostic accuracy and predictive value of each clinical characteristic for confirmed Ebola virus disease.

Findings Between May 29, 2014, and Dec 8, 2014, 850 patients with suspected Ebola virus disease were admitted to the holding unit, of whom 724 had an EBOV RT-PCR result recorded and were included in the analysis. In 464 (64%) of these patients, a diagnosis of Ebola virus disease was confirmed. Fever or history of fever (n=599, 83%), intense fatigue or weakness (n=495, 68%), vomiting or nausea (n=365, 50%), and diarrhoea (n=294, 41%) were the most common presenting symptoms in suspected cases. Presentation with intense fatigue, confusion, conjunctivitis, hiccups, diarrhea, or vomiting was associated with increased likelihood of confirmed Ebola virus disease. Three or more of these symptoms in combination increased the probability of Ebola virus disease by 3·2-fold (95% CI 2·3–4·4), but the sensitivity of this strategy for Ebola virus disease diagnosis was low. In a subgroup analysis, 15 (9%) of 161 confirmed Ebola virus disease cases reported neither a history of fever nor a risk factor for Ebola virus disease exposure.

Interpretation Discrimination of Ebola virus disease cases from patients without the disease is a major challenge in an outbreak and needs rapid diagnostic testing. Suspected Ebola virus disease case definitions that rely on history of fever and risk factors for Ebola virus disease exposure do not have sufficient sensitivity to identify all cases of the disease.

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Introduction

The scale of the ongoing Ebola virus disease outbreak in parts of west Africa is unprecedented, with an estimated cumulative incidence of 27 049 cases and 11 149 deaths by May 27, 2015.[1] Sierra Leone is the most severely affected country so far. The first case in Sierra Leone was confirmed on May 25, 2014, in Kailahun district in the Eastern Province.[2] By Oct 22, 2014, all 14 of Sierra Leone's districts had been affected.[3] A peak incidence of 537 cases per week was reported in the week ending Nov 30, 2014.[1] Although the incidence fell dramatically from early December, 2014, to late March, 2015, at the time of going to press, Ebola virus disease transmission continues in three districts in Sierra Leone.[1]

A key component of the Ministry of Health and Sanitation (MoHS) of Sierra Leone's operational plan for country preparedness was the establishment of isolation facilities referred to as Ebola holding units at every hospital facility.[4,5] Connaught Hospital in Freetown is Sierra Leone's main adult referral hospital, providing inpatient and outpatient medical and surgical services, and an emergency department, and accepts unselected cases from the community and referrals from other health centres. In May, 2014, Connaught Hospital Ebola holding unit was opened, staffed by the MoHS and volunteers from the King's Sierra Leone Partnership, a capacity-building partnership with King's Health Partners in London, UK, based at Connaught Hospital since 2013. Whereas many other health facilities were forced to close during the Ebola outbreak because of inadequate infection control measures, Connaught Hospital remained open throughout 2014, largely

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Research in context

Evidence before this study

We searched PubMed for published articles since the year 2000 using the search terms "Ebola" AND each of "symptom", "screen", and "predict" on Nov 3, 2014, and later on April 10, 2015 (with no starting date restriction), with the search terms "Ebola" AND each of "prediction", "clinical presentation", and "diagnosis". Relevant articles were identified through the use of summary information and abstracts. The full text of relevant articles was obtained. We identified several studies that reported on the clinical features of Ebola virus disease cases, including large studies from the present outbreak and smaller studies from previous outbreaks. However, only two studies compared the clinical features of confirmed Ebola virus disease cases with suspected cases that tested negative for the disease. In the first of these, Maganga and colleagues reported on a cohort of suspected cases in the 2014 Ebola virus disease outbreak in the Democratic Republic of the Congo, comparing Ebola virus disease-negative cases with probable and confirmed cases. Most (11/16) of the clinical features reported were predictive of the disease in this cohort, including fever, headache, vomiting, malaise, diarrhoea, muscle pain, difficulty swallowing, and conjunctivitis. A recent study by Levine and colleagues of 382 patients with suspected Ebola virus disease presenting to an Ebola treatment centre in Bong County in rural Liberia reported that a positive contact history, diarrhoea, anorexia, muscle pain, and difficulty swallowing were predictive of Ebola virus disease diagnosis. A six-point Ebola prediction score was derived, validated internally, and was recommended for patient prioritisation at Ebola holding units or treatment centres. An earlier study by Pittalis and colleagues analysed the accuracy of the WHO case definition for Ebola haemorrhagic fever by retrospectively applying it to published clinical descriptions of Ebola virus disease cases occurring before March, 2008. The authors showed a low sensitivity (58·5%) of the WHO definition for Ebola virus

disease diagnosis in published cases and called for a high index of clinical suspicion to identify cases. Dananche and colleagues assessed the fever threshold used in case definitions in non-epidemic areas and recommended that this threshold be reduced.

Added value of this study

Our study reports predictive symptoms for Ebola virus disease diagnosis in a large cohort of suspected cases presenting to the adult referral hospital in Freetown, from urban and rural areas of Sierra Leone. Our study uniquely shows that inclusion of fever or history of fever and risk factors for Ebola virus disease exposure in existing case definitions for Ebola virus disease reduces their sensitivity and might contribute to missed cases, which could result in onward transmission to health-care workers in a general health-care setting. Additionally, our study shows the variability in Ebola virus disease predictive features in comparison to previous reports, with implications for the design of a screening device.

Implications of all the available evidence

Inappropriate case definitions and delayed recognition of Ebola virus disease cases might have contributed to early failure of disease control in the current west African outbreak. As this outbreak recedes, methods of screening for Ebola virus disease cases in health-care settings are being debated by policy makers. The possibility of Ebola virus disease resurgence in west Africa remains. Rather than reduce the sensitivity of screening tools in favour of more specific approaches, maintenance of isolation units at health facilities and universal training of health-care workers in Ebola virus disease identification and infection prevention are key to successful outbreak control. Highly sensitive and specific rapid diagnostic tests for Ebola virus disease are urgently needed.

because of its ability to triage patients with suspected Ebola virus disease into the holding unit.

Ebola holding units are distinct from Ebola treatment centres in that they admit people with possible or suspected, rather than just confirmed, Ebola virus disease, and refer patients on to treatment centres once the diagnosis has been confirmed. In many cases, they are located at an existing health-care facility such as that at Connaught Hospital. They are the point of access to basic health care for many patients with febrile illness in the outbreak setting and provide initial empirical treatment for common causes of febrile illness and access to Ebola virus disease diagnostic testing.

In the context of an outbreak in which extremely high health worker infection rates were being reported, it was imperative to identify, isolate, and test individuals with suspected Ebola virus disease before allowing them access to routine health services such as emergency departments,

general wards, or outpatient clinics.[6,7] Screening algorithms to identify Ebola virus disease cases are typically based on suspected Ebola virus disease case definitions, such as those provided by WHO, which are adapted locally as the outbreak develops (panel).[8] However, the accuracy of this approach for Ebola virus disease diagnosis in symptomatic patients presenting at local health-care facilities in an Ebola virus disease outbreak had not been formally assessed before the present west African outbreak. One study had previously reported on the low sensitivity of the WHO case definition when retrospectively applied to published Ebola virus disease case descriptions.[9] Several other studies have emphasised the difficulty in distinguishing Ebola virus disease from other causes of febrile illness.[10–15] Some reports have suggested that Ebola virus disease case identification in health facilities was not robust in the early months of the ongoing and previous Ebola virus disease outbreaks and