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Group work: case definition

Working group summary

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Introduction

- 17 experts from WHO, regulators, clinicians, epidemiologists, clinical trialists from Nigeria, Ghana, Liberia, Guinea, USA, Benin and South Korea.
- Primary Objective: To decide on case definition to capture most cases (epidemiological case finding with high sensitivity).
- Secondary Objective: To decide on key variables to collect for clinical trial case definition.
- Starting point: Draft WHO case definition for clinical case management (updates by the working group are highlighted)

Definitions

- Suspected Lassa fever case: History of fever or fever for > 48hours, but <21 days

- Probable case:
- ➢ Death or loss to follow up of suspected case with no Laboratory confirmation.

- Confirmed case: Laboratory confirmed Lassa fever by positive RT-PCR

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Fever

- Any history of fever
- Any temperature ≥ 38°C (Brighton Collaboration)
- Measured by Axillary or non-contact thermometer (during outbreaks)
  - Measurement by both methods with comparison of recordings could be done outside outbreak season.
- Duration: 48 hours or more but less than 21 days.

AND any of the following additional Symptoms

- Any symptom: sore throat, malaise, headache, cough, myalgia, nausea, vomiting diarrhea, retrosternal pain, hearing loss, early signs of bleeding e.g. conjunctival bleeding, woman with abnormal vaginal bleeding; OR
- Any complications, such as encephalopathy (seizure, coma, irritability, confusion), shock, bleeding, acute kidney injury; OR
- Pregnant woman with spontaneous abortion, post-partum hemorrhage, intrauterine fetal demise, sepsis; OR
- Travel to endemic area within past 21 days plus contact with rodents; OR
- Contact with LF patient or probable case within past 21 days
- Source: WHO

Severity

Severe case:

- Any complications, such as encephalopathy (seizure, coma, irritability, confusion), shock, bleeding, acute kidney injury; AND/OR
- Abnormal LFT, RFT, Coagulation profile.
- Grading of additional symptoms by functional impairment.
- Pregnant woman with spontaneous abortion, post-partum hemorrhage, intrauterine fetal demise, sepsis.

Moderate and Mild cases:

- TBD based on retrospective analysis of clinical and laboratory data obtained during epidemiological study.
- Dito other parameters indicative of severity.

Other considerations

- Dipstick for early severity identification (proteinuria and haematuria) in the field.
- Standardized collection of symptoms via the epi study will allow for later case definition variations for clinical trials.
- Individual case management protocols might include testing for co-infections or alternative diagnosis.
- Data on co-infections and co-morbidities should be collected.
- Feedback received on priority ranking of additional symptoms will be analyzed and collated.
- Functional laboratory tests e.g. hematocrit, platelet count and liver function tests could help refine the case definition and possibly ascertainment for the clinical trials.

Post-workshop review

The initial case finding Lassa Fever case definition should be opened up:

A confirmed Lassa fever case to be defined as:

- Febrile illness with temperature ≥ 38°C for 48 hours and up to 21 days OR a history of fever OR
- Illness clinically suspected to be Lassa Fever by the Investigator with a positive RT-PCR

Post-workshop review (2)

This will likely require

- Field use of rapid diagnostic tests for initial screening
- Significant laboratory capacity building

Post-workshop review (3)

Clinical signs & symptoms:

- Clinical evaluation will be performed for additional signs and symptoms as per WHO case definition
- These data will be collected in a standardized manner to allow refinement and performance assessment of case definitions for future epidemiological and clinical trials
- Laboratory testing will be done for confirmation of LF as well as clinical labs (minimum liver and renal function tests, coagulation profile)
- Local standards of care may require additional tests, based on clinical presentation and at medical discretion