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No: F.1-22/Advisory/CDC/2023 *Islamabad, 10th November 2023*

Subject: Awareness and Alert communication for Human Leptospirosis

Background:

Leptospirosis is a rare zoonotic bacterial disease caused by the bacterium belonging to *Leptospira* genus, transmits from animals mostly rodents, pets, cattle and other wild animals to humans through contact with infected animal excreta. Animals that are natural hosts to a particular pathogen usually show no or comparatively few ill effects after infection with Leptospira.

Objectives of the Awareness letter:

The objective of this communication is to alert and facilitate the health authorities and other stakeholders for ensuring early detection, timely management and laboratory detection of Leptospirosis cases.

Epidemiology and Clinical Presentation:

Leptospirosis occurs worldwide but is more common in tropical and subtropical areas with high rainfall. In recent years, cases of human and animal leptospirosis have been reported in numerous countries in the Middle East. However, sporadic cases are reported in Pakistan since past few years. The disease is found mainly wherever humans come into contact with the urine of infected animals or a urine-polluted environment. It is an occupational hazard for many people who work outdoors or with animals or water-based activities. Person-to-person transmission is very rare, there may be individuals who have been exposed to a common source (co-exposed).

The infection is highly variable, ranging from asymptomatic to self-limited febrile illness to severe disease. The incubation period is 5-14 days but may extend up to 30 days in some cases. Symptoms include fever, headache, chills, vomiting, abdominal pain, diarrhea, cough, jaundice, anemia, or rash. Severe muscle aches (calves and lumbar region) and conjunctival suffusion are specific findings but are less commonly observed. Patients with active infection, if left untreated, may present with aseptic meningitis, pulmonary hemorrhage, respiratory insufficiency, myocarditis, and impaired hepatic and renal function.

Case Definitions

WHO case definitions for suspected, probable and confirm cases are as below:

Suspected Case:

Any person presenting with clinical signs and symptoms consistent with leptospirosis: abrupt onset of fever, chills, conjunctival suffusion, headache, myalgia, jaundice, cardiac or renal failure, and pulmonary haemorrhage with exposure history; Cyclone and/or flooding or exposure events such as adventure sports and water-based activities.

Probable:

Any suspected case and the presence of Leptospira immunoglobulins type M (IgM) in one serum sample detected by serology (e.g. Immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA)).

Confirmed Case:

A suspected case is confirmed by laboratory tests as follows:

Sero-conversion or a four-fold or higher rise in titre detected by serological techniques (e.g. microscope agglutination technique (MAT) 2 or IgM ELISA) in consecutive serum samples; or detection of Leptospira DNA from a clinical specimen by polymerase chain reaction (PCR); or demonstration of Leptospira spp. in tissue.

Laboratory Confirmation:

Following laboratory tests can be done for the confirmation of Leptospirosis:

- **Dark Field Microscopy**: This can be used to visualize the Leptospirosis, however due to less sensitivity it has not been considered as a gold standard test to rule out the diseases.
- **ELISA (IgM & IgG):** This test is widely used for the confirmation of Leptospirosis but it has the disadvantage of having false positive results due to low specificity. Moreover, as antibodies can persist in blood for many years and the titer of antibodies cannot be detected in the early phase of disease.
- **Microscopic Agglutination Test (MAT):** This test is used as a gold standard test with high specificity for sero-diagnosis of leptospirosis. However, it is less sensitive during the early phase of disease. This test requires a great deal of expertise, a long and complicated procedure to maintain the strain for preparing live antigen. Acute and convalescent serum samples collected 7–14 days apart is ideal. If only one serum sample can be sent for testing, a sample collected after the first 7–10 days of illness is preferred.
- **Polymerase Chain Reaction (PCR):** It is useful for detecting DNA in serum and blood during the first week of infection. However, this test is much more expensive and requires a large quantity of DNA. This test cannot identify the infecting serovar. Whole blood collected in the first week of illness (in the first 4 days is ideal), urine (collected at least 1 week after symptom onset is ideal), cerebrospinal fluid from a patient with signs of meningitis, fresh frozen kidney and/or liver (if available from deceased patients, kidney preferred).
- **Immunohistochemistry:** This test can also be done, Formalin-fixed tissues from different organs like kidney (preferred), liver, lung, heart, or spleen.

Case Management:

Appropriate use of antibiotics in symptomatic patients may decrease the severity and duration of illness. In patients with leptospirosis, initiating antibiotic treatment as soon as possible without waiting for laboratory results is recommended. Doxycycline is the drug of choice (100 mg orally, twice daily), if not contraindicated. Other options include azithromycin (500 mg orally, once daily), ampicillin (500-750 mg orally, every 6 hours), amoxicillin (500 mg orally, every 6 hours). Intravenous (IV) penicillin is the drug of choice (1.5 MU IV, every 6 hours), and ceftriaxone (1 g IV, every 24 hours) can be equally effective for the patients with severe illness.

Prevention and Control Measures:

Following preventive measures are recommended for limiting the Leptospirosis transmission:

- Promote public awareness of possible transmission risk when undertaking recreational water-based activities including wading, swimming and white water rafting.
- Use of appropriate protective equipment for the staff working in hazardous occupations in order to prevent contamination, including when working with potentially infected animals, their tissues or secretions.
- Water-proof dressing on cuts and abrasion while working in the water-based activities and encourage frequent hand washing during exposure to high risk settings or environments.
- Implement rodent control measures around homes, buildings and other work related areas attracting rodents.
- Animal handlers should seek veterinary advice about preventing leptospirosis in companion animals or livestock.

Surveillance Measures:

Early detection of pathogen and identification of likely source of infection so that the likelihood of further cases from the same source can minimize the risk of disease transmission in others. It is therefore recommended to be vigilant and report any suspected/confirm case to concerned authorities.

This risk communication letter may please be widely distributed among all concerned to keep NIH posted about the measures undertaken in respective areas of jurisdiction.

(Dr. Muhammad Salman)
Chief Executive Officer

Distribution Overleaf

Distribution:

1. Secretary, Health Department, Government of the Punjab, Lahore
2. Secretary, Health Department, Government of Sindh, Karachi
3. Secretary. Health Department, Government of KPK, Peshawar
4. Secretary, Health Department, Government of Balochistan, Quetta
5. Secretary, Health Department, Government of AJK, Muzaffarabad
6. Secretary, Health Department, Government of Gilgit-Baltistan, Gilgit
7. Chief Executive Officer, Islamabad Healthcare Regulatory Authority, Islamabad
8. Chief Executive Officer, Punjab Healthcare Commission, Lahore
9. Chief Executive Officer, Sindh Healthcare Commission, Karachi
10. Chief Executive Officer, KPK Healthcare Commission, Peshawar
11. Director General Health Services, Government of the Punjab, Lahore
12. Director General Health Services, Government of Sindh, Hyderabad
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15. Director General Health Services, Government of Gilgit-Baltistan, Gilgit
16. Director General Health Services, Government of AJK, Muzaffarabad
17. Director General, National Health Emergency Preparedness and Response Network (NHEPRN), Islamabad
18. Animal Husbandry Commissioner, M/o National Food Security & Research, Islamabad
19. Executive Director, Pakistan Institute of Medical Sciences, Islamabad
20. Executive Director, Federal Government Polyclinic Hospital, Islamabad
21. Executive Director, CDA Capital Hospital, Islamabad
22. Executive Director, Federal Government TB Hospital, Rawalpindi
23. Executive Director, National Institute of Rehabilitation Medicine (NIRM), Islamabad
24. Director General Health Services, Capital Development Authority, Islamabad
25. Director General, PAEC Hospital, Islamabad
26. Director General, KRL Hospital, Islamabad
27. Director General, NESCOM Hospital, Islamabad
28. Director, Border Health Services-Pakistan, Islamabad
29. District Health Officer, ICT, Islamabad
30. Director, Nuclear Oncology & Radiotherapy Institute (NORI), Islamabad
31. Commandant, PAF Hospital, Islamabad
32. Commandant, Naval Complex Hospital, (PNS Hafeez), Islamabad
33. Medical Superintendent, Social Security Hospital, Islamabad
34. Director, Federal General Hospital, Park Road, Islamabad
35. Executive Director, Shifa International Hospital, Islamabad
36. Executive Director, Qauid-e-Azam International Hospital, Islamabad
37. Executive Director, Maroof International Hospital, Islamabad
38. Commandant, Combined Military Hospital (CMH), Rawalpindi
39. Commandant, Military Hospital (MH), Rawalpindi
40. Medical Superintendent, Cantonment General Hospital, Rawalpindi
41. Medical Superintendent, District Headquarter Hospital, Rawalpindi
42. Medical Superintendent, Fauji Foundation Hospital, Rawalpindi
43. Medical Superintendent, Holy Family Teaching Hospital, Rawalpindi
44. Medical Superintendent, Benazir Bhutto Hospital, Rawalpindi
45. Medical Superintendent, WAPDA Hospital, Rawalpindi
46. Medical Superintendent, Railway Hospital, Rawalpindi
47. In-charge, Federal Disease Surveillance Unit (FDSRU), NIH Islamabad
48. Officer In-charge, Provincial Disease Surveillance Unit (PDSRU) at Provincial Health Directorates, Lahore, Hyderabad, Peshawar, Quetta, Gilgit and Muzaffarabad
49. Deputy Commissioners with the request to direct all concerned departments at district level.

Copies to:

1. Chief Secretary, Govt of Punjab, Sindh, KPK, Balochistan, GB and AJK.
2. Surgeon General Pakistan Army, GHQ Rawalpindi
3. Chief Commissioner, ICT Administration Islamabad
4. WHO Country Representative, Islamabad
5. SPS to Federal Minister of Health, M/o NHSR&C, Islamabad
6. SPS to Secretary, M/o NHSR&C, Islamabad
7. PS to Director General Health, M/o NHSR&C, Islamabad