ORIGINAL ARTICLE

Kyasanur Forest Disease: Clinical profile, diagnostic approaches, and management protocol

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Abstract

Background: Kyasanur Forest Disease (KFD) is an emerging tick-borne flavivirus first identified in 1957 in Karnataka, India. Since 2012, the disease has expanded to four other states, posing an increasing public health threat. This study aims to develop a comprehensive, standardized protocol for clinical characterization, diagnostic approaches, and management of KFD to assist clinicians and public health specialists in navigating its expanding geographical footprint and reducing associated mortality. **Methods:** With the involvement of multiple experts and their experiential learnings in managing the KFD cases, this comprehensive protocol was developed emphasizing on clinical presentation and management. **Results:** KFD poses a significant public health challenge with a mortality rate ranging from 2% to 10%, and reported higher fatality in non-endemic regions. The disease typically presents with an abrupt onset of fever, severe headache, myalgia, and prostration, progressing to a biphasic course in 10-18% cases. Haemorrhagic and neurological complications, including altered sensorium, seizures, and meningitis, can occur and are associated with increased mortality with multi-organ dysfunction syndrome (MODS). Diagnosis relies on molecular methods (RT-PCR, real-time RT-PCR) and serological assays (IgM/IgG ELISA). Currently, no specific antiviral treatment is available, and management is primarily supportive, focusing on symptom control, fluid balance, and addressing complications. **Conclusion:** The current manuscript consolidates current knowledge on the epidemiology, clinical characteristics, differential diagnosis, laboratory investigations, and management strategies for KFD primarily for the clinician and public health specialist. This also

highlights the critical need for early diagnosis, robust surveillance, and improved supportive care to reduce morbidity and mortality.

KEYWORDS
Kyasanur Forest Disease; clinical management; diagnosis; protocol; India

INTRODUCTION

Kyasanur Forest Disease (KFD), commonly known as "monkey fever," is a zoonotic disease caused by the Kyasanur Forest Disease virus (KFDV), a pathogenic arbovirus belonging to the family *Flaviviridae* [1]. An investigation into a large-scale death of monkeys in 1957 led to the initial identification of the disease in the Kyasanur forest of the Shimoga district in Karnataka. In nature, the virus is maintained mainly in *Heamaphysalis* ticks, mammals and birds which primarily affect humans and monkeys. Humans acquire the infection primarily by bite of infected tick nymphs. The deaths of the monkey indicate active transmission zones. Handling monkey carcasses may pose an indirect risk because of the risk of bite from infected tick still attached to the body of the deceased monkey or exposure to tick infested areas during carcass retrieval. KFD transmission is seasonally observed during the months of October to May when *Haemaphysalis* tick nymphs are on questing activity. This is the time that needs increased vigilance and preventive measures in endemic and neighboring districts. Populations that have direct interactions with forests, i.e., tribal populations, farmers, forest workers, and cashew nut/areca nut cultivation workers, fire-wood collectors, animal grazers, hunters, trekkers, etc. are also at the greatest risk because of the frequent occupational exposure to areas with ticks. Mortality trends demonstrate that the case fatality rates might vary (2-10%) [1] and be reportedly higher in non-endemic areas (newer), as the one is not diagnosed promptly and lacks pre-existing immunity in the population. With an average of 400 to 500 reported cases annually, KFD has been a persistent public health concern in India since its initial identification. The outbreaks and scattered cases are mostly from five districts in Karnataka State: Uttara Kannada, Chikmagalur, Dakshina Kannada, Shimoga and Udupi [1]. Apparently from the year 2012, KFD cases started detecting from the new areas, either involving monkey deaths or human cases from Chamarajanagar district (2012), Karnataka State, Mudumalai Tiger Reserve, Tamil Nadu State (2012), Wayanad and Malappuram districts, Kerala State (2013–2015, 2019, 2020), Goa (2015–2024), and from Sindhudurga district of Maharashtra State (2016–2025) [1-10]. Moreover, the socio-ecological factors, such as deforestation, land-use alterations, and heightened human-wildlife-tick contact, are known to drive the development of KFD in new geographic foci, thus permitting the transmission of the virus between the sylvatic cycle and humans [11]. This geographical spread underscores the changing epidemiology of KFD and emphasis for enhancing the surveillance and preparedness in new regions of Western Ghats.

Although a formalin inactivated KFDV vaccine has been long employed in endemic regions, its production and use were stopped in October 2022 in India because of the poor efficacy, manufacturing difficulties, and failure to comply with the regulatory standards [12-14]. Since there is currently no antiviral or broadly accessible vaccine, personal protection (e.g., tick repellents, protective clothing) and controlling the vectors now have to be the priorities of primary prevention. Besides this, no specific anti-viral therapy for KFD is available. The infected cases are mainly managed with supportive therapy.

For effective clinical management and disease surveillance, an accurate and timely diagnosis is of great importance. Molecular and serological assays, including nested RT-PCR, real-time RT-PCR, and KFD IgM and IgG ELISA, have been instrumental in the identification and surveillance of KFDV. This manuscript thus aims at offering a systematic, evidence-based and experiential yet exhaustive review of clinical manifestation, diagnostic methods and the prevailing management options of KFD

with extensive emphasis on informing clinicians and public health professionals.

Material & Methods

Following extensive consultations with multidisciplinary experts during the period January 2025 to July 2025, this protocol was refined to incorporate best practices and current evidence. The case definition, diagnostic algorithms, clinical management of the cases included in this protocol are derived from published literature, national and World Health Organization (WHO) guidelines, and refined through the authors' direct clinical and laboratory experience in managing KFD cases.

Ethical statement

This manuscript presents a clinical and management protocol developed through expert consensus and synthesis of existing evidence and experiential learnings from clinicians involved in the management of Kyasanur Forest Disease cases. It does not involve primary research on human participants, human samples, or identifiable data; therefore, institutional ethical approval and informed consent were not required.

Results

Integrating the insights from multidisciplinary experts with established clinical evidence, the following sections present the standardized framework for KFD management, ranging from initial clinical characterization to specific treatment protocols

Clinical characterization

Incubation period: The incubation period of KFD in humans is estimated to be 2 to 7 days after tick bites or exposure [1,11]. In up to 18% of cases, the disease follows a biphasic course, with a second phase often occurring after a 1 to 2-week afebrile period [15].

Signs and symptoms: KFD is a biphasic illness. The onset of the first phase is abrupt, beginning with chills and progressing to a severe frontal headache. Fever can escalate to as high as 104°F (40°C) and persists for about 3-9 days (mean 6.3 ±3 days) [13]. Severe myalgia, often likened to dengue fever, is a prominent feature, with body aches particularly pronounced in the nape of the neck, lumbar region, and calf muscles.

The clinical features are different in two phases of illness. The first phase presents with fever, myalgia, headache (40%) and other constitutional symptoms. Patients may have arthralgia, abdominal pain, vomiting, or diarrhoea. Diarrhoea and vomiting may develop by the third or fourth day of illness [15].

During the initial phase of illness, physical examinations reveal a febrile patient with severe prostration. Conjunctival suffusion is common. The cervical lymph nodes may be palpable [16]. A frequent feature is the appearance of macular or maculopapular lesions on the soft palate (enanthem), and diffuse maculo-papular rashes on the body. Petechiae, ecchymosis may be seen in patients with coagulopathy. Hypotension is observed in a proportion of patients at hospital presentation. Abdominal examination may reveal hepatosplenomegaly. Patients developing complications may also show hepatic dysfunction with jaundice and decreased urine output. Haemorrhagic manifestations, such as bleeding from the nose (epistaxis), gums, and intestines, can occur as early as the third day. However, the majority of cases resolve without significant haemorrhagic symptoms. Patient may present with vomiting of blood (haematemesis), a sign of upper gastrointestinal (GI) bleeding or fresh blood in the stools, (haematochezia), which indicates lower GI bleeding. Some patients may experience a persistent cough with blood-tinged sputum, and, rarely, significant haemoptysis (coughing up blood). Other sites of bleeding are oral cavity bleeding, intracranial haemorrhage and in women, vaginal bleeding or polymonorrhagia. Haemorrhagic manifestations are seen in 8% of patients with KFD [15,16].

In the first phase of the illness, up to 10% of hospitalized patients may experience significant neurological complications such as altered sensorium, seizures, and coma, which have been linked to increased mortality [15,17]. With the exception of intracranial haemorrhage, focal neurological deficits are uncommon in the first phase.

KFD complications include pneumonitis, which can progress to acute respiratory distress syndrome (ARDS). Other reported complications are myocarditis, pancreatitis, and hepatitis, which can sometimes advance to fulminant hepatitis and hepatic encephalopathy. Acute kidney injury is also a possible complication [17]. The second phase of the illness, if it occurs, may be characterised by a resurgence of headache (100%), fever (neurological abnormalities such as aseptic meningitis, asthenia (weakness), tremors, delirium, convulsions, and focal neurological deficits such as cerebellar signs. Haemorrhagic manifestations can rarely be reported in the second phase. While the neurological manifestation in the first phase is due to encephalopathy or encephalitis, in the second phase it is usually due to meningitis, meningoencephalitis and cerebellar dysfunction.

The two phases show distinct laboratory features. The first phase is associated normal or elevated haemoglobin because of haemoconcentration or anemia because of bleeding or underlying nutritional cause. Characteristically there will be leucopenia and thrombocytopenia in the first phase whereas in the second phase there will be normal white blood cells or leucocytosis, and thrombocytopenia is rare. Similarly, elevated bilirubin, liver enzymes, creatine kinase, are observed in the first phase, they are primarily normal during the second phase [15,17]. In the first phase, activated partial thromboplastin time (aPTT) is elevated, while prothrombin time (PT) remains normal; however, in the second phase, both coagulation parameters are normal. In the first phase, severe cases might have disseminated intravascular coagulation, indicated by high prothrombin time (PT), aPTT, and low fibrinogen levels. The CSF analysis during the second phase reveals aseptic meningitis with lymphocytic predominance, elevated proteins and normal glucose.

The reported deaths are commonly observed during the first phase of the illness in about 2-10% of hospitalized patients. Causes of death can be refractory shock, myocarditis, ARDS, diffuse alveolar haemorrhage, gastrointestinal haemorrhage, fulminant hepatic failure, multi organ dysfunction and secondary bacterial sepsis. In a tertiary care retrospective study of hospitalized patients, independent predictors of mortality in the first phase included lower Cycle threshold (Ct) values, older age, lower respiratory tract involvement, altered sensorium, and elevated white blood cell counts [18]. Death is very rare in the second phase. The people who survive usually recover without neurological deficits. The convalescent phase of KFD is often prolonged with persistent generalized weakness, and reduce appetite.

Differential diagnosis: The clinical similarity of KFD to other endemic infections requires the exclusion of the common co-circulating pathogens, particularly those common in the Western Ghats area. Differential diagnoses should be classified by clinical syndrome:

- **Acute Undifferentiated Febrile Illness:** Chikungunya, Malaria, Typhoid fever.
- **Hemorrhagic Fevers:** Dengue, Crimean-Congo Hemorrhagic Fever (CCHF), Leptospirosis, Scrub Typhus, Omsk haemorrhagic fever (OHF)
- **Neurological Infections:** Japanese Encephalitis, West Nile Virus, Zika virus disease, Tick-borne encephalitis (TBE), Lyme disease, Bacterial Meningitis.

The clinical overlap necessitates careful consideration of the patient's epidemiological history and timely laboratory confirmation to distinguish KFD from these other conditions.

Case definition: Given the variability in clinical illness associated with KFD infection and the scarcity of definitive clinical diagnostic criteria, laboratory testing is paramount for accurate case ascertainment. The following case definitions are proposed with modifications in earlier available case definition The case definitions used following are according to the guidelines of the Directorate of Health and Family Welfare Services (Government of Karnataka), and have been changed to provide greater sensitivity to outbreak detection in new foci [1]:

Suspected Case: A person of any age presenting with acute onset of fever with any of the following: headache, myalgia, prostration, generalized weakness, nausea, vomiting, diarrhoea, and occasionally

neurological or haemorrhagic manifestations. AND associated with any of the following risk factors:

- Lives in the forests of an endemic area.
- Recent visit to an endemic area* during the past 2 weeks.
- Recent visit to an area with unexplained monkey deaths.
- History of occupational engagement in forests of an endemic area during the past 2 weeks.

*Endemic area: An area which has reported positivity in human or monkey viscera or tick pools in the last 5 years.

Probable Case: A clinically similar presentation that does not meet the criteria for a confirmed definition but has one of the following features:

- Epidemiological link to a documented exposure to a KFD-affected area (one or more of the following exposures within 2 weeks before onset of symptoms).
- Positive result on immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) testing of clinical serum specimens.

Confirmed Case: A confirmed case of KFD is defined as a case that meets the criteria for a probable KFD case and, in addition, should cover any of the following:

- Detection of KFDV-specific genetic sequence by reverse transcription-polymerase chain reaction (RT-PCR) or real-time RT-PCR from blood or tissues.
- Isolation of KFDV in cell culture or in a mouse model, from blood or tissues.

Screening of the suspected cases: Serological or molecular testing is necessary to exclude other differential diagnoses, as detailed in the "Differential Diagnosis" section.

Diagnostic workflow at different healthcare levels: To ensure early detection and systematic management, a stratified diagnostic approach is implemented across the healthcare hierarchy, guiding clinicians from initial screening to advanced critical care interventions

At Primary/Community health centers

Patients presenting at primary or community health centers should undergo an initial screening and basic investigations to detect hematological abnormalities. The following steps are recommended [Figure-1]:

- Complete Blood Count (CBC): Includes Total Leukocyte Count (TLC), Differential Leukocyte Count (DLC), Hemoglobin (Hb), and Platelet count. This helps in identifying leukopenia, thrombocytopenia, and reduced hemoglobin (Hb) levels.
- If abnormalities are detected (leukopenia, thrombocytopenia, or reduced Hb):
    - Liver Function Test (LFT): Assesses hepatic involvement.
    - Coagulation Profile: Evaluates blood coagulation status.
    - Renal Function Test (RFT): Assesses renal involvement.

At tertiary care centers

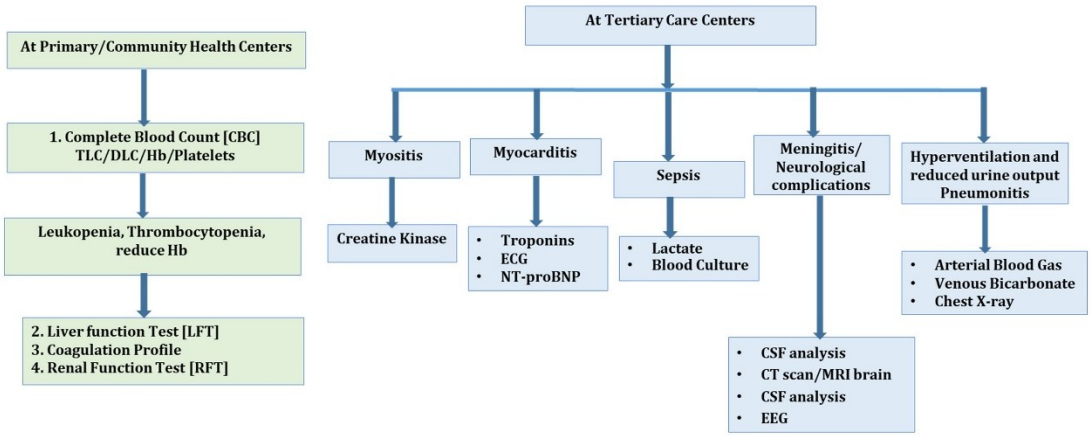
Patients requiring comprehensive evaluation or those with severe symptoms or complications are referred to tertiary care centers, where advanced investigations are performed, depending on the clinical presentation [Figure-1]:

- Myositis:
    - Creatine Kinase: measured to assess muscle involvement and diagnose myositis.
- Myocarditis:
    - Troponins: indicates myocardial injury
    - Electrocardiogram (ECG): Evaluates cardiac rhythm and detects myocarditis
    - NT-proBNP: assesses heart failure.
- Sepsis:
    - Lactate: Indicates tissue hypoperfusion and metabolic stress.
    - Blood Culture: Identifies the causative organism and blood samples to be collected prior to antibiotic administration.
- Meningitis/Neurological Complications:

- Cerebrospinal Fluid (CSF) Analysis: to identify infectious or inflammatory causes
- CT Scan/MRI Brain: to detect structural or inflammatory brain involvement.
- Electroencephalogram (EEG): to evaluate functional brain abnormalities.

- Hyperventilation, Reduced Urine Output, Pneumonitis:
  - Arterial Blood Gas (ABG): Assesses respiratory function and acid-base balance.
  - Venous Bicarbonate: Evaluates metabolic status,
  - Chest X-ray: Detects pulmonary involvement.

This stepwise approach ensures systematic evaluation of patients based on the level of healthcare facility and clinical presentation, allowing for timely detection and management of hematologic, hepatic, renal, muscular, sepsis, cardiac, neurological, and respiratory complications.



Laboratory diagnosis:

- **Real-time RT-PCR:** This is the first-line test for KFD, recommended during the acute stage of infection (1-24 days) from human blood/serum [16]. KFD RT-PCR is also utilized for testing dead infected monkey blood and viscera, or tick tissues during surveillance activities [19-21].
- **IgM ELISA:** The IgM ELISA test can be used to identify KFD antibodies starting from the fourth day of illness, which is a sign of a recent infection [19].
- **IgG ELISA/ Neutralization Tests:** These are applied to the diagnosis of past infections (paired sera) and in serosurveillance when it is necessary to determine whether a previously naïve area has any infected individuals.

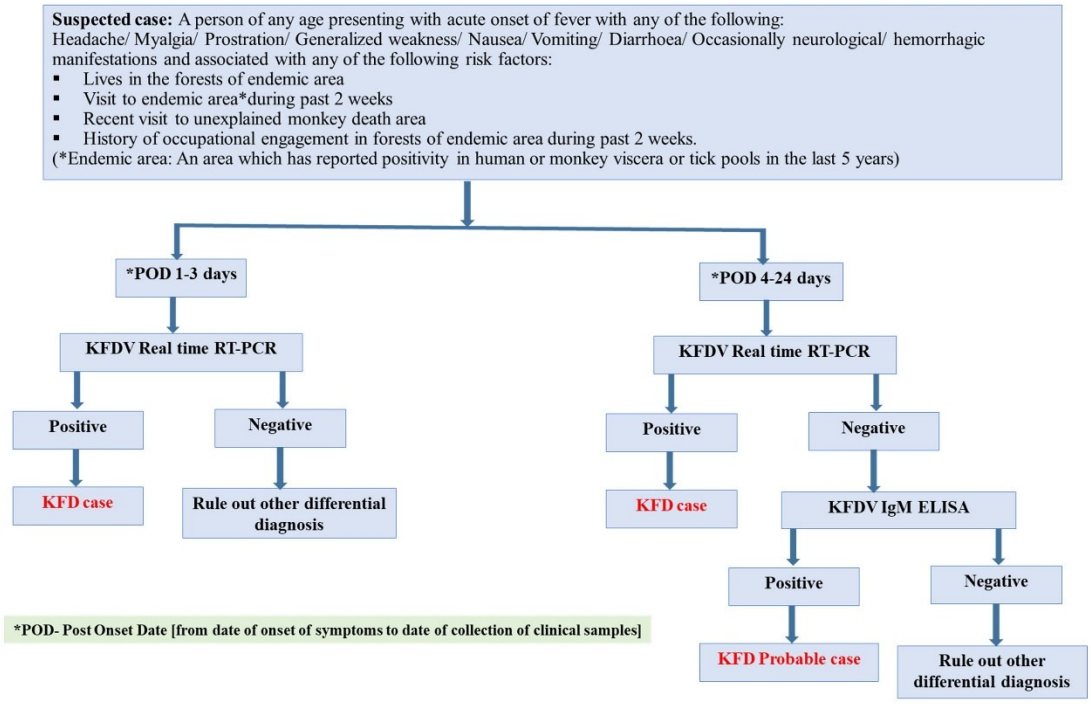
Table 1 summarizes the major differences in clinical and laboratory features of the two phases to make easier reference.

Table 1: Comparison of Clinical and Laboratory Features in KFD Phases

Feature	First Phase (Days 1-8)	Second Phase (Weeks 3-4)
Clinical Symptoms	Sudden high fever, severe headache, myalgia, prostration, hemorrhagic manifestations (in severe cases).	Recurrence of fever, severe headache, meningeal signs, tremors, mental status changes.
Pathophysiology	Viremia, cytokine storm.	Immune-mediated / Inflammatory response.
Hematology	Leukopenia, Thrombocytopenia.	Normal WBC (or leukocytosis), Normal Platelets.
Diagnostic Test	RT-PCR Positive.	IgM and IgG antibodies Positive.

Biosafety, specimen handling, and transport

During sample collection and processing, strict compliance with the biosafety measure is obligatory. Handling of all specimens should be done in accordance with risk group-2 equivalent precautions [22]. The staff should use the right personal protective equipment (PPE) such as N95 masks, gloves, and gowns. Any biological waste produced during the sampling process should undergo decontamination and should be disposed of in accordance with the biomedical waste management regulations [22]. The detailed standard operating procedures (SOPs) must be rigorously followed at each hospital ward and laboratory to ensure proper specimen collection. The Blood samples should be collected by the treating physician or a trained phlebotomist via venipuncture using an aseptic technique from the hand or antecubital fossa. 5-6 ml of blood samples should be collected and distributed into EDTA, SSGT (Serum Separator Gel Tube), Citrate, and Heparin tubes as per the desired serological and hematological tests. Transportation of clinical samples should comply with the WHO/ International Air Transport Association recommendations on the transport of Infectious Substances (Category B) [23]. The samples must be transported under cold chain (2–8°C) using triple layer packaging system. The transit time to the testing laboratory must be no longer than 24-48 hours. The diagnostic algorithm to be followed for testing of suspected KFDV cases [Figure-2].



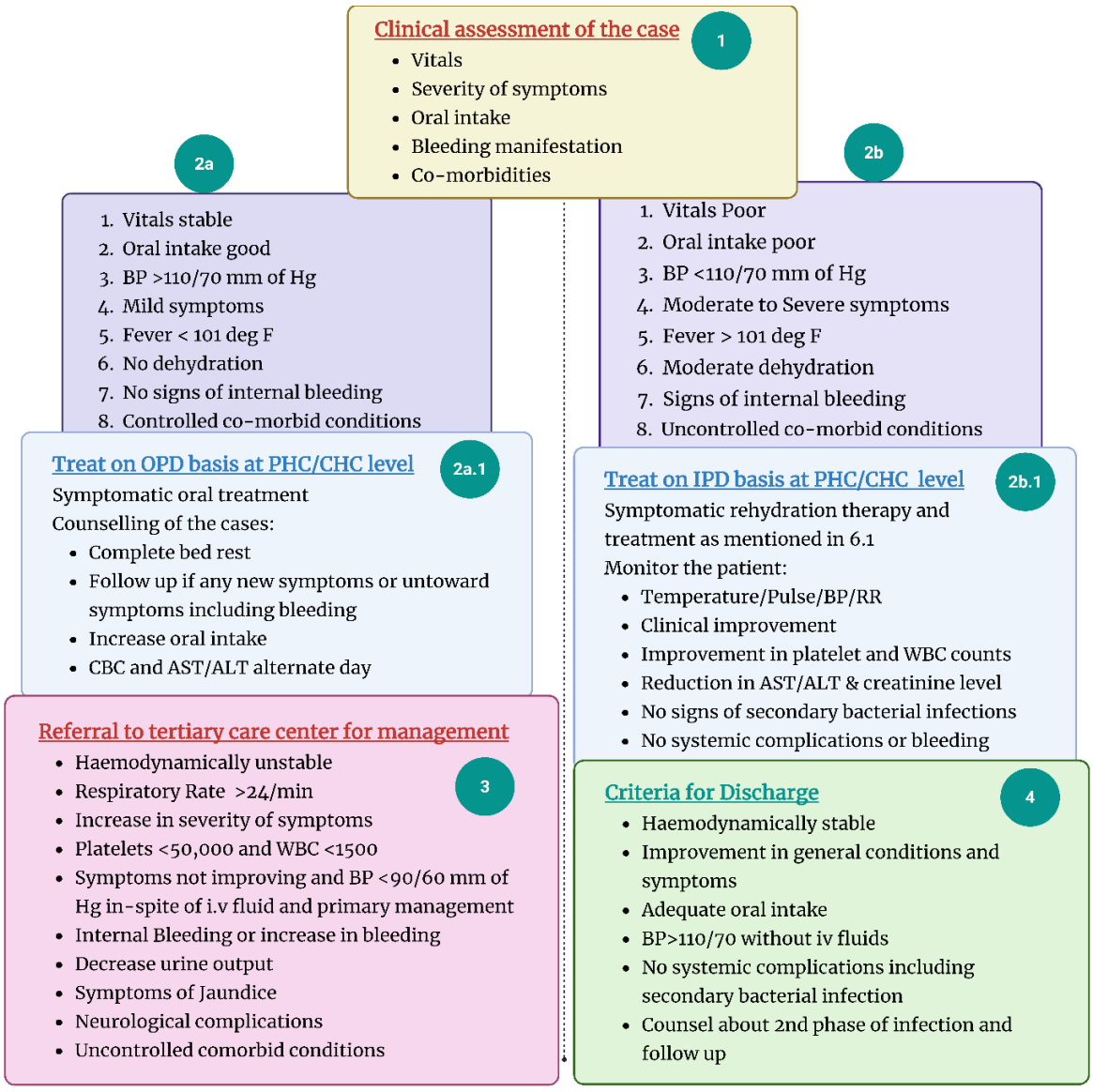
Surveillance and reporting workflow

Proper surveillance requires a well-organized reporting process. The positive laboratory results of KFD are to be reported to the District Surveillance Unit (DSU). The data is then channeled to the State Surveillance Unit (SSU) where the information is updated in Integrated Health Information Portal (IHIP) under the Integrated Disease Surveillance Programme (IDSP) of the National Centre for Disease Control (NCDC). This will guarantee real time, thorough surveillance loop in response to outbreaks.

Clinical management of KFD cases

The management of KFD is purely supportive because no specific antiviral treatment is currently available. This involves managing symptoms, maintaining hydration, and using standard precautions for patients who have bleeding disorders. At the Primary Health Centre (PHC) level and Community Health Center (CHC) level- including Rural Hospital

(RH) and Sub-district hospital (SDH), the clinical management of KFD cases is stratified based on the patient's presenting signs, symptoms, and potential complications. Initial assessment encompasses vital signs, symptom severity, oral intake status, evidence of bleeding, and co-morbidities. Patients presenting with stable vitals, adequate oral intake, mild symptoms, and no overt signs of dehydration or internal bleeding are typically managed on an outpatient department (OPD) basis, focusing on symptomatic relief, bed rest, and close monitoring with follow-up complete blood count (CBC) and liver function tests. Conversely, individuals exhibiting clinical deterioration, characterized by poor vitals, compromised oral intake, moderate to severe symptoms, dehydration, or signs of internal bleeding, necessitate inpatient department (IPD) care at the PHC. This involves intensive symptomatic rehydration therapy and meticulous monitoring of physiological parameters and laboratory markers. Critically, any patient displaying hemodynamic instability, progressive symptom severity, significant thrombocytopenia or leucopenia, refractory hypotension despite intensive fluid resuscitation, persistent bleeding, neurological sequelae, or uncontrolled co-morbidities mandates immediate referral to a higher-level facility for advanced medical intervention. This tiered approach optimizes resource utilization at the PHC while ensuring timely escalation of care for complicated KFD presentations [Figure-3].



Recommended treatment symptomatic KFD cases:

As KFD is a viral illness, its management is primarily supportive, focusing on the alleviation of symptoms, correction of physiological derangements, and prevention/treatment of secondary complications. This document outlines a structured approach to the symptomatic management of KFD cases, based on common clinical presentations.

Fever, headache, severe myalgia, malaise [24]:

- Paracetamol (Acetaminophen): 0.5–1g every 4–6 hourly, with a maximum of 4g daily, until symptoms abate. Dosage should be adjusted based on patient weight and age. Caution is advised in patients with liver abnormalities or altered liver enzymes.
- Tramadol: 50-100 mg every 8 hourly for severe myalgia. (Oral/Intravenous)
- Tepid sponging: To help reduce fever.
- Non-steroidal anti-inflammatory medications NSAIDS should be avoided.

Nausea and vomiting:

- Antiiemetics such as
  - Metoclopramide: 5–10 mg intravenously (IV) single dose.
  - Domperidone: 10 mg orally three times daily (tid) half an hour before meals.
  - Ondansetron: 8 mg IV twice daily (bd).
- Stress ulcer prophylaxis/gastritis
  - Pantoprazole: 40 mg orally once daily (od), may be given IV
  - Ranitidine 150 mg twice daily oral or IV
- Intravenous fluids: Administer if the patient has prostration or dehydration and is unable to take oral fluids.

Secondary infections:

- Broad-spectrum antibiotics is indicated if super-added bacterial infection is suspected, particularly in hemodynamically unstable patients. Examples include Inj Ceftriaxone 1g IV od or Piperacillin Tazobactam 4.5g IV tid or other antibiotics based on local antibiogram. Blood cultures are to be requested before starting antibiotics.

Haemorrhagic diathesis:

- Vitamin K: 10mg/day IV for 3 days.
- Tranexamic acid: 500mg orally or IV three times daily for 5-7 days if active bleeding is present.
- Prophylactic platelet transfusions are not definitively recommended for patients with a platelet count of <50,000 platelets/microlitre who have no active bleeding [20]. Such transfusions are only suggested for non-bleeding patients with a platelet count <10,000/µL, or for invasive procedures.

Altered sensorium, irritability, and seizures:

- Mannitol 20%: Administer every 8 hourly (age-wise dosage based on body weight is recommended) for cerebral oedema. Mannitol should be avoided in cases of decreased urine output or renal failure. In such scenarios, 3% NaCl or Furosemide (Lasix) 20 mg can be considered.
- Levetiracetam: 20-60 mg/kg IV at 2-5 mg/kg/min if the patient experiences seizures. Dose modification is required in renal failure.
- Lorazepam/Diazepam: Can be used to terminate active seizures.

Electrolyte imbalance/Hyponatraemia and acidosis:

- Intravenous fluids: Administration of Sodium chloride or Ringer Lactate depending on the degree

of dehydration and the patient's general condition.
- Metabolic acidosis: If present, it needs to be evaluated and treated, particularly if the pH is less than 7.1.

Fluid refractory hypotension/Shock [25]:
- Norepinephrine: 0.2 to 1.5 µg/kg/min (5-30 µg/min).
- Vasopressin: Up to 0.03-0.04 units/min, or Epinephrine: 0.01 to 0.5 µg/kg/min in adults (5-15 µg/min), may be considered as second-line agents if norepinephrine is insufficient.

Referral of the patient to a higher centre:

If the patient presented with any of the following signs or symptoms, it should be immediately taken o tertiary care centre:
- Refractory Shock: Hemodynamic instability despite initial fluid resuscitation.
- Severe Thrombocytopenia: Platelet count <50,000/µL with or without active bleeding.
- Neurological Manifestations: Altered sensorium (Glasgow Coma Scale < 13), seizures, or focal neurological signs.
- Multi-Organ Dysfunction: Evidence of acute kidney injury (oliguria/anuria) or severe liver dysfunction.
- Co-morbidities: Uncontrolled pre-existing conditions (e.g., severe diabetes) complicating management.
- Blood pressure (BP) less than 90/60 mm of Hg (even after IV fluids)
- Persistent heart rate >100/min, Irregular pulse
- Respiratory rate greater than 24 breaths/min
- Altered sensorium
- Significant bleeding manifestations
- Decreased urine output
- Jaundice
- Severe dehydration
- Uncontrolled co-morbid conditions
- White blood cell count less than 1500/µL

Note: The administration, dosage, and duration of medicines/drugs are determined by the patient's clinical condition. The treating physician or specialist retains the authority to make decisions regarding the course of treatment and management.

Discussion

KFDV remains a significant public health challenge in India, with its expanding geographical footprint and potential for severe outcomes. The lack of specific antiviral treatment underscores the critical importance of early diagnosis, aggressive supportive care, and robust surveillance. It is crucial for clinicians in both endemic and newly affected areas to consider the possibility of KFD in patients who present with an acute fever and a history of relevant exposure. Non-specific febrile illness may however be more common in children requiring a high index of suspicion in endemic countries in order to avoid delays in diagnosis and worse prognoses. While comprehensive data on pediatric KFD is limited, available literature shows that the clinical course of infection among children is similar to that among adults. [26]. Standardized case definitions, timely laboratory confirmation through molecular and serological assays, and comprehensive supportive clinical management are crucial for better patient outcomes. Clinicians should also be alert to co-infections (e.g. KFD with malaria or leptospirosis or typhoid fever) especially during the post-monsoon seasons when there is overlapping of vectors. The co-infection also may modify the course and severity of the clinical presentation, which makes it harder to diagnose and provide supportive treatment.

Mitigating the burden of KFD and preventing future outbreaks requires key actions such as further research into antiviral treatments, newer vaccine development, and enhancing preparedness strategies. This protocol is designed for healthcare providers who are responsible for identifying and treating patients with KFDV infections, and it can be

used at all levels of the healthcare system. The protocol will also be used as a resource by policymakers, health managers, and health facility administrators to help develop national, regional, and local guidelines for clinical management. In conclusion, this protocol provides a gap in the current literature as it synthesizes multi-centers experience learning and recent epidemiological changes- namely the extension to Maharashtra, Goa and Kerala. It also offers a standardized, up-to-date method of diagnosis and management in both established and newer endemic areas that has a significant gap in existing clinical guidelines.

Authors Contribution

RRS, DYP, KS, TC, JP, MM, AMS, NG, PDY contributed to protocol writing, data interpretation, and critical review. All authors contributed to the critical review and finalization of the paper. The authors' extensive clinical experience in managing patients with Kyasanur Forest Disease in India, alongside their active involvement in the establishment and validation of laboratory diagnostic methods, underpin the development of this comprehensive clinical protocol.

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Conflict of Interest

There are no conflicts of interest.

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Declaration Of Generative AI And AI Assisted Technologies In The Writing Process

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