found.

Kidneys in the early stages are spared. Renal failure are documented in the later stages due to complications. Multi-organ failure is usually found in the severe stages of the disease.

4.3. Post Nipah infection complications:

Psychiatric complications may be seen after full recovery. If the neurological signs and symptoms of encephalitis develop after more than 10 weeks of the initial exposure, it is known as late-onset encephalitis. Long term complication are seen in some case in the form of relapse of encephalitis months to years after recovery.

4.4. Laboratory Diagnosis

Laboratory diagnosis of a patient with a clinical history of NiV can be made during the acute and convalescent phases of the disease by using a combination of tests.

Laboratory confirmation of NiV infection either by:

i) IgM antibody against NiV identified in serum or CSF,
ii) NiV RNA identified by RT-PCR from respiratory secretions, urine or cerebrospinal fluid, or
iii) Isolation of NiV from respiratory secretions, urine or cerebrospinal fluid or other tissue specimens (only to be carried out in a BSL 4 Laboratory).

Tests at sr.No. (i) and (ii) can be carried out in a BSL 2 laboratory carrying BSL 3 precautions.

As it is a BSL -4 pathogen, the specimen collection and the triple layer packaging requires well trained staff. The procedure of sample collection and packaging is placed at **Annexure-I.**

4.5. Treatment

4.5.1. Guiding Principles

There is no confirmed effective specific treatment for NiV infection in humans to date. The guiding principles are:

- Early implementation of infection control precautions will minimize nosocomical/ household spread of disease.
- Active surveillance, contact tracing and early identification and follow up of persons at risk. Surveillance case definition is placed at **Annexure-II.**
- Provision for dedicated isolation facilities for patients must be created so that laboratory confirmed Nipahcases as well as suspect cases are either kept in individual isolation rooms or cohorted (separate ward for keeping confirmed and suspect cases) in a well ventilated isolation ward with beds kept at-least one metre apart.
- Community contacts and hospital contacts who have gone back to the community are kept in home quarantine. Hospital staff may be kept in home quarantine or in separate individual isolation room facility in a hospital.
- Suspect and probable cases should be hospitalized in isolation facility as described above.
- There should be dedicated doctors, nurses and paramedics well trained in hospital infection control practices and following the standard, contact and droplet precautions to attend to the suspect or confirmed cases.Reinforce standard infection control precautions for all those entering the room must use hand washing practices, high efficiency masks, gowns, goggles, gloves, cap and shoe cover.
- Imaging and laboratory investigations are to be limited till such time laboratory reports are available. This would reduce the risk of transmission of disease among Health Care Workers.
- The isolation facility should have portable X Ray machine, ventilators, large oxygen cylinders, pulse oxymeter and other supportive equipments.
- Adequate quantities of PPE, disinfectants and medications are to be ensured.
- **No accompanying relative or friends of the patient is to be allowed in isolation facility**. Restrict number of visitors and those allowed to visit should be providedwith full protection through PPE.

- Dispose bio medical waste properly by placing it in sealed impermeable bags labelled as Bio- Hazard after decontamination with 5% Sodium Hypochlorite.
- The commonly touched surfaces in the isolation ward should be cleaned with freshly prepared disinfectant (5% Sodium Hypochlorite) every 4 hours.
- Hand sanitizers should be provided at every bed post and exit part of the isolation rooms.
- Any hospital staff getting contaminated should discard the PPE and take a bath immediately with soap and hot water.

4.5.2. General management

- Symptomatic and supportive treatment should be started immediately in all clinically suspected cases. Maintain airway, breathing and circulation (ABC).
- Ensure patient isolation (preferably in a separate ward/room).
- Institute barrier nursing, e.g., personal protection using masks, gloves, gowns, shoe covers and hand-washing with soap and water before and after handling/visiting patients.

4.5.3. Symptomatic and supportive treatment:

a. Patient is advised to drink plenty of fluids.
b. Fluid maintenance and electrolyte balance.
   Fluid restriction, after initial resuscitation, is advisable in order to avoid fluid overload/ complication
c. Nasogastric tube feeding/ parenteral nutrition may be instituted, if necessary.
d. Paracetamol is suggested for fever, myalgia and headache.Salicylate / aspirin is strictly contra-indicated in any Nipah patient due to its potential complications.
e. The cases would be constantly monitored for clinical / radiological evidence of lower respiratory tract infection and for hypoxia (respiratory rate, oxygen saturation, level of consciousness).
f. Patients with signs of tachypnea, dyspnea, respiratory distress and oxygen

saturation less than 90 per cent should be supplemented with oxygen therapy. Types of oxygen devices to be used would depend on the severity of hypoxemia. It can be started from oxygen cannula, simple mask, partial re-breathing mask (mask with reservoir bag) and non re-breathing mask. Disposable cannula only should be used for Oxygen inhalation. In children, oxygen hood or head boxes can be used.

g. Oropharyngeal or endotracheal suction when used should mandatorily be done using a closed suction circuit to avoid dispersal of aerosol in the environment.

h. Patients with severe pneumonia and acute respiratory failure (SpO2 < 90% and PaO2 <60 mmHg with oxygen therapy) must be supported with mechanical ventilation. Invasive mechanical ventilation is preferred choice. Non invasive ventilation is an option when mechanical ventilation is not available. Protocol for management of respiratory failure is given at **Annexure-III.**

i. Anticonvulsants e.g., intravenous diazepam,phenobarbitone, phenytoin or levetiracetam may be used in the standard recommended doses.Mannitol could be used in case of raised Intracranial tension.

j. Suspected cases does not require antibiotic therapy. Antibacterial agents should be administered, if required, as per locally accepted clinical practice guidelines. If required, patients on mechanical ventilation antibiotics should be used judiciously to prevent hospital associated infections.

k. Patients requiring Vasopressors for shock may be started on noradrenalin infusion with or without dobutamine in cases with significant cardiac dysfunction.

l. Use of steroids have not been shown to be effective in managing the neurological/ respiratory involvement.

4.5.4. Drug therapy:

Ribavirin:

As currently there are no strong evidence of proven therapy, it is advisable to administer Ribavirin to all confirmed cases of Nipah virus infection as per the available limited in vitro and in vivo evidences, **subject to approval of Drug Controller General of India [DCG(I)].**

Ribavirin is not a proven treatment for Nipah, and has only single open label trial evidence from Malaysia. But the benefit was significant with 36% reduction in mortality. Therefore, in absence of other treatments, and considering its safety profile, quite well in short term as well as longer experiences with Hepatitis C patients it has been recommended for use in confirmed Nipah infections.The suggested dosesare based on the WHO Guidelines for other hemorrhagic fevers, such as Lassa, Crimean Congo etc.

Dose for Ribavirin

For Adults

- 2000 mg loading (10 tabs of 200 mg)
- Day 1-4 - 1000 mg 6hrly (5 tabs of 200 mg each 4 times daily for 4 days = 80 tablets)
- Day 5-10- 500 mg 6hrly (200 mg each tablet 3 tab - 3 tab - 2 tab - 2 tab at 6hrs gap daily for 6 more days = 60 tablets)

For Children

- Load 30mg/kg,Thereafter,
- for Day 1- 4 to give15 mg/kg 6hrly
- Day 5- Day 10 to give 7.5 mg/kg 6 hrly.

On an average each patient (adult) would require 150 capsules for a 10 days course.

Parentral dose of Ribavirin.

IV Ribavirin

- loading dose of 30 mg/ kg
- then 15 mg / kg every six hourly for 4 days
- Then 7.5 mg / kg every eight hourly for 6 days.

Ribavirin should be diluted in 150 ml of 0.9% Normal Saline and infused slowly.

Adverse reactions of Ribavirin:

Serious Reactions can include haemolytic anaemia, neutropenia, thrombocytopenia, aplastic anaemia, teratogenicity, embryocide, severe depression, suicidal ideation, autoimmune disorders, pulmonary toxicity, pancreatitis, diabetes, hypothyroidism, hyperthyroidism, myocardial infarction, arrhythmias, colitis, retinal haemorrhage, retinal thrombosis, or rarely, hypersensitivity reactions.

Common Reactions can include fatigue, headache, fever, rigors, myalgias, arthalgias, anxiety, irritability, insomnia, alopecia, neutropenia, nausea, vomiting, anorexia, depression, pruitis, dizziness, dyspnoea, anaemia, diarrhea, impaired concentration, cough, rash, or thrombocytopenia.But most adverse drug reactions are in long term therapy as seen in Hepatitis C, not common as in short term therapy.

4.5.5. Newer experimental drugs:

(i) Favipravir has recently been shown to be effective against Nipah viral infections in animal model.

(ii) Immunomodulating drugs have not been found to be beneficial in treatment of ARDS or sepsis associated multi organ failure. High dose corticosteroids in particular have no evidence of benefit and there is potential for harm.

4.5.6. Post Exposure Prophylaxis:

There is no evidence to support the role of ribavirin as post-exposure prophylactic treatment for Nipah fever.

Human monoclonal antibody:

Human Monoclonal antibodies targeting the viral glycoproteins(**anti-G MAb or**