Clinical management of patients with Ebola virus disease

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Clinical management of patients with Ebola virus disease
A number of clinical care guidance documents have been produced by organisations with EVD experience. Such guidelines and recommendations have been informed by published observational studies and case reports, as well as specific hands-on experience and expert opinion. This guidance document represents a synthesis of international and country-specific guidelines. The management of EVD requires a team approach, with input from specialists with expertise in critical care, infectious diseases, obstetrics, laboratory medicine and infection control amongst others.

Overview: the clinical course of EVD
There appear to be four phases of EVD, which often overlap (Table 1).

Table 1. Clinical features of Ebola Virus Disease

<table>
<thead>
<tr>
<th>Phase of illness</th>
<th>Time since symptom onset</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early febrile</td>
<td>0-3 days</td>
<td>Fever, malaise, fatigue, body aches</td>
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</table>
| Gastrointestinal       | 3-10 days                | **Primary**: epigastric pain, nausea, vomiting, diarrhoea<br>
                          |                          | **Associated**: persistent fever, asthenia, headache, conjunctival injection, chest pain, abdominal pain, arthralgias, myalgias, hiccups, delirium |
| Shock or recovery      | 7-12 days                | **Shock**: diminished consciousness or coma, rapid thread pulse, oliguria, anuria, tachypnoea<br>
                          |                          | **Recovery**: resolution of gastrointestinal symptoms, increased oral intake, increased energy |
| Late complications     | ≥10 days                 | Haemorrhage (most commonly gastrointestinal haemorrhage), secondary infections, meningoencephalitis, persistent neurocognitive abnormalities |

The following clinical features of EVD should be noted:

- Haemorrhage is not a prominent sign or symptom in most patients with EVD; in an observational study of >700 EVD patients in Liberia, clinically significant haemorrhage occurred in <5% of patients. Severe thrombocytopenia is common.

- Patients can have a waxing and waning clinical course. The phenomenon of unexpected, unexplained precipitous deterioration in seemingly stable patients has been a common finding during this outbreak. Young patients tend to appear compensated longer before rapid declines.

- Diarrhoea may be profuse, with large volumes of watery diarrhoea (≥5 litres per day), and vomiting may be severe and recurrent. Severe diarrhoea and vomiting results in profound water and electrolyte depletion, and ultimately hypovolaemia and shock. Data from Sierra Leone show that patients initially present with hyponatraemia, hypokalaemia, hypocalcaemia, and elevated creatinine and urea levels indicative of dehydration. However, hypernatraemia has also been recorded.
  - The mechanism of Ebola-mediated diarrhoea has not been characterised, but is thought to be secretory with possibly a minimal inflammatory component.

- The pathophysiological features of shock and multi-organ failure reported in severe EVD appear to differ from the pathophysiology of sepsis in other critically ill patients in ICU settings. While pro-inflammatory mediators may contribute to vascular leak, hypotension and organ failure in severe EVD, these patients present with minimal clinically appreciable capillary leak (i.e. peripheral or pulmonary oedema), and acute hypoxaemic respiratory failure is distinctly uncommon.

- Since malaria is endemic in West African countries affected by the outbreak, synchronous malaria infection must be urgently and rigorously excluded. Where delays may occur, empiric antimalarial treatment should be considered.

- Hepatocellular injury marked by aminotransferase elevation is very common in EVD and raised alkaline phosphatase is often seen, but liver failure is an uncommon complication. Hypoalbuminaemia is reported.

- It appears that secondary bacterial infection/sepsis is an uncommon manifestation or complication. Theoretically, there is a risk of bacterial translocation during the gastrointestinal phase of illness, particularly when diarrhoea is severe; for this reason, the use of appropriate antibiotics, such as intravenous ceftriaxone 1g od, to cover potential enteric pathogens if new onset fever or clinical deterioration occurs is a reasonable approach.
Diagnosis of EVD
Due to the general unavailability of approved specific therapies for EVD it is essential to make a diagnosis as soon as possible in order to initiate supportive measures before the development of irreversible pathology (particularly shock) and to institute adequate infection control procedures.

Ebola virus is detected in blood usually only after onset of symptoms.

Within a few days after clinical onset, laboratory tests that may be used include: detection of the virus antigen by antigen capture enzyme-linked immunosorbant assay (ELISA), detection of IgM antibody by ELISA, detection of nucleic acid by real time polymerase chain reaction (RT-PCR), and virus isolation in tissue cultures or laboratory animals.

Later in disease course or after recovery laboratory confirmation of EVD infection can be achieved by testing for specific IgM and IgG antibody.

Post-mortem diagnosis if required is based on immunohistochemistry testing (skin punch and liver biopsy specimens), RT-PCR and virus isolation (skin punch and liver biopsy specimens)

Principles guiding the clinical management of EVD patients
Since there are no approved treatments available for EVD, the clinical care of patients is primarily supportive.

Patients with confirmed EVD should be cared for in a setting capable of intensive and frequent monitoring of vital signs, fluid balance and neurologic status. Since aggressive supportive care has the potential to increase survival, the patient should be cared for in an ICU setting. Numerous patients that have been treated in ICU settings who developed severe multi-organ dysfunction and required ventilator and dialysis support, have recovered.

General Principles and Infection Control
The overarching principle is that patients must receive the care they require while ensuring safety of staff. To achieve the following need to be considered:

- Safety of staff is critical
- Minimise direct physical contact with patient.
  - only staff trained and with access to suitable PPE should have direct physical contact with the patient
minimise exposure by limiting the number of staff dealing with the patient

- Only essential invasive procedures should be undertaken
- All clinical activities should ideally be planned and performed by staff who are well versed in the specific activities
- Consult with the Infectious Disease Unit early, and transfer to such a unit if appropriate.

**Clinical examination and assessment**

- Intensive and frequent monitoring of vital signs, respiratory rate, fluid balance and neurological status
- Manage pre-existing co-morbidities

**Monitoring**

- Non-invasive monitoring
  - Cardiorespiratory monitoring (including heart rate, ECG, respiratory rate, oxygen saturation and non-invasive blood pressure) must be available for all EVD patients.
  - Finger-prick glucose
  - Urine output
  - Sequential weight assessment may be a useful index for fluid management, particularly if the patient has substantial unmeasured fluid losses due to diarrhoea or insensible losses. However the difficulty of weighing these sick patients may require assessment based on input/output and vital signs alone.
  - Daily FBC and U&E & creatinine with LFT and INR at baseline and follow up if any bleeding, jaundice or hepatomegaly

- Invasive monitoring
  - Arterial blood pressure monitoring should be considered in select cases with haemodynamic instability requiring vasoactive agents and frequent blood test monitoring.
  - Central line access may be considered if aggressive potassium replacement is required or when there is difficulty obtaining peripheral venous access due to oedema. If a central line has been established, the use of CVP monitoring can be considered. Central line access for purposes of CVP monitoring alone is not recommended.
Clinical management recommendations

Principles of EMS Care and transport
Staff safety remains of utmost importance when EMS facilitates transport of a suspected or confirmed Ebola patient. To be able to minimise risk the following should be done:

- Contact with the patient should be kept to a minimum number of providers
- Only staff with training in the correct usage of appropriate PPE, and who have been issued such PPE, should be doing such transfers
- Fluid therapy is a critical step; if needed, commence IV fluids at the earliest opportunity.
- Placement of IV lines and any other resuscitation procedures are best done prior to loading the patient into an ambulance.
- Invasive procedures must not be done in a moving ambulance – the risk to the attending medical crew is too high.
- Oral antiemetics should be considered prior to transport.
- EMS crew should at all times remain in contact with their supervising medical officer

Emergency care
Although a standard ABC approach following the primary survey and resuscitation / secondary survey and emergency treatment method is required, note that the main emphasis during initial emergency care is on IV access and fluid loading, with electrolyte management and early administration of ceftriaxone.

- **Airway management and ventilation**
  - The airway may need to be protected, for example in the setting of decreased level of consciousness or massive upper GI bleeding
  - Pulmonary involvement is not a common feature of EVD. Secondary causes of respiratory failure may necessitate mechanical ventilation; such causes may include shock, fatigue from prolonged compensation of metabolic acidosis, secondary bacterial infection, and iatrogenic complications (e.g. transfusion-related lung injury)

- **Fluid and electrolyte management**
  - Administration of fluids and electrolytes remains the first step in supportive care interventions. Persistent fluid and electrolyte losses often require ongoing fluid and electrolyte replacement.
  - There are no studies specific to the treatment of patients with EVD to guide fluid management strategies; consider the following expert recommendations:
Peripheral IV access is suitable for fluid management. Large bore IVs are preferred to allow large volume fluid resuscitation should the patient suddenly deteriorate. Should there be an indication for central line access (when aggressive potassium replacement is required or when there is difficulty obtaining peripheral venous access), this may also be used for fluid management.

The amount of IV fluid administration should be guided by the degree of overt volume loss (diarrhoea, vomiting and urine) as well as indicators suggestive of volume contraction (decreased skin turgor, dry mucous membranes, tachycardia, decreased urine output, and hypotension).

Ringer’s lactate (RL) is recommended as the fluid of choice for volume replacement. For hypotensive patients, initial boluses of RL of 20mL/kg should be commenced and repeated as required, until the heart rate, blood pressure and parameters of end-organ perfusion are within the desired range. Pulmonary oedema has been noted after excessive fluid resuscitation. When large volumes of crystalloid solutions are administered, consider using albumin. Artificial colloids (e.g. pentastarch or hydroxyethyl starch) should be avoided given their associated risks of renal injury and bleeding.

Consider administration of blood and blood products when a patient is haemorrhaging or the haemoglobin is approaching 7g/dL. Consider transfusion of platelets and coagulation factors in patients who have serious bleeding, or are at high risk for bleeding, or require invasive procedures. Platelets should be administered to patients with a platelet count of <20 x 10⁹/L or if <50 x 10⁹/L and associated with serious bleeding. If serious bleeding is occurring and INR >2, fresh frozen plasma (FFP) should be administered, or Hemosolvex factor IX (Prothrombin complex concentrate) if volume overloaded. If the fibrinogen level is low in the face of significant haemorrhage (particularly if <2g/L), cryoprecipitate should be transfused.

Electrolyte replacement:

Significant electrolyte deficiencies (particularly hypokalaemia, hyponatraemia, and metabolic acidosis secondary to bicarbonate loss) occur in patients with vomiting and/or voluminous diarrhoea. However, hypernatraemia may occur in some patients.

Oral replacement of electrolytes is effective if tolerated.
- Consider adding potassium and bicarbonate to maintenance IV fluids early for patients with diarrhoea to prevent severe hypokalaemia (assuming no evidence of renal failure) and metabolic acidosis.
- Hypocalcaemia is common, and frequently requires aggressive replacement with calcium gluconate.
- Should concentrated IV electrolyte replacements be needed, central line access is indicated.
- Electrolyte replacement should be guided by serum values; regular testing of serum sodium, potassium, bicarbonate, creatinine, glucose, lactate, calcium, magnesium and phosphate is recommended.
  - Vasopressors:
    - Hypotensive patients who don’t respond to fluid resuscitation should be supported with vasopressor therapy as per standard guidelines for the management of septic shock.

**Organ support**
  - Severely ill patients may progress to organ failure requiring extracorporeal support. Any decision for extracorporeal support must take into account any baseline coagulopathy.
  - Renal failure is common in severe cases, and dialysis should be considered if indicated; the mode of dialysis should be individualised based on the patient’s status and the treating clinician. The use of continuous renal replacement therapy offers the advantage of minimising the need for additional staff to enter the patient’s room if this therapy is routinely managed by the critical care nurses. The US CDC has developed a document on recommendations for safely performing acute haemodialysis in patients with Ebola virus disease – available at: [http://www.cdc.gov/vhf/ebola/healthcare-us/hospitals/acute-hemodialysis.html](http://www.cdc.gov/vhf/ebola/healthcare-us/hospitals/acute-hemodialysis.html).
  - Liver dysfunction progressing to liver failure is a major consideration for severe EVD.
  - The use of extracorporeal membrane oxygenation (ECMO) for cardiorespiratory failure has not been reported in severe EVD, and is not recommended.

**Prophylaxis and preventive measures for the critically ill**
  - Routine strategies for avoiding nosocomial infections should be instituted.
  - Stress ulcer prophylaxis with either a histamine-2 receptor antagonist, sucralfate, or a proton-pump inhibitor if actively bleeding is recommended for mechanically ventilated patients, given that GI bleeds are frequent in severe EVD.
The benefit of deep-vein thrombosis prophylaxis must be carefully considered, given the possibility of coagulopathy occurring with EVD. Severe thrombocytopenia is a further contraindication. Use of stockings should be considered.

- Vigilant monitoring for secondary bacterial infection
  - Patients should be regularly monitored for signs of infection by means of laboratory tests (e.g. CRP), clinical, and where indicated, radiological assessments. This is particularly important when the clinical condition deteriorates. Clinicians are encouraged to consult with clinical microbiologists and infectious disease specialists as to appropriate empiric antimicrobial therapy and approach to investigation for suspected secondary infections.

Symptomatic care
Symptoms should be controlled early and throughout the course of illness. Effective symptom management is a significant component of the supportive care strategy. An approach to the management of several common symptoms is shown in Table 2.

Table 2. Management of common symptoms of Ebola virus disease

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Management</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, chills, headache and myalgias</td>
<td>Paracetamol</td>
<td>Avoid non-steroidal anti-inflammatory drugs (NSAIDs) due to their platelet-inhibiting effects which could exacerbate haemorrhage</td>
</tr>
<tr>
<td>Pain (involving abdomen, chest wall, headache and joint pain) not adequately managed with paracetamol alone</td>
<td>Narcotics, morphine, fentanyl</td>
<td></td>
</tr>
<tr>
<td>Severe diarrhoea</td>
<td>Consider use of loperamide</td>
<td>Recent expert opinion advises considering the use of loperamide in patients with profuse voluminous diarrhoea, with the following cautions: ○ Avoid when ileus or intestinal paresis suspected or documented</td>
</tr>
</tbody>
</table>
Presumptive care
Pre-emptive antibiotics: the use of appropriate antibiotics at first diagnosis in sick patients with potential secondary bacterial infection is recommended. A low threshold for antibiotic use to cover translocating Gram-negative bacteria from the gut is advised should the patient’s condition deteriorate in keeping with sepsis.
If, for any reason, malaria testing is delayed, consider empiric antimalarial therapy until malaria investigation results are available and synchronous malaria infection confidently excluded.

Nutritional support
In patients with less severe disease, oral rehydration fluid should be provided. Frequent smaller volume meals may be better tolerated. Prophylactic anti-emetic medication should be used to encourage oral intake.

- Oral nutritional supplements should be considered for those patients with suboptimal intake.
- NG tube placement with enteral feeds should be considered for patients that can’t safely swallow.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe vomiting</td>
<td>NG tube and suction Metoclopramide, ondansetron</td>
<td>Generally not recommended for use in children but has been used in children &gt;2 years of age</td>
</tr>
<tr>
<td>Hiccups</td>
<td>Consider enteral nutrition via NG tube Symptomatic management with chlorpromazine</td>
<td>Common in severe cases</td>
</tr>
<tr>
<td>Agitation / confusion</td>
<td>Consider diazepam, haloperidol</td>
<td></td>
</tr>
</tbody>
</table>
• Intubated patients should have early nasogastric tube placement with initiation of enteral feeds
• Patients with diarrhoea may experience worsening of their symptoms with enteral feeds; in such cases, consider feeds with lower osmolality or semi-elemental feeds
• Enteral feeds are preferred to parenteral nutrition
• Early consultation with a dietician is recommended

**Psychosocial support**
Psychosocial support services for both the patient and their family must be provided.

**Drug Therapy**
Although no drug therapy has been proven to be of value, it is recommended that attempts be made to access certain specific therapies, which may include:

• Immune serum: derived from convalescent patients and is currently recommended as a therapy by WHO
• ZMAPP: a combination of 3 humanised monoclonal antibodies to 3 Ebola virus glycoprotein epitopes and engineered for expression in tobacco plants.
• Antiviral drugs
  • Favipiravir – designed as an anti-influenza drug, which has shown to cure EVD in mice. Selectively inhibits viral RNA-dependent RNA polymerase. Human trials are due to start in West Africa
  • Brincidofovir – Currently undergoing phase III trials for cytomegalovirus and adenovirus. It has also shown activity against Ebola virus in vitro. It has been used in patients with EVD in the US as an emergency drug. Trials are planned in West Africa.
• [Other drugs]
  • Amiodarone, clomiphene and chloroquine have some antiviral effect and will be trialed in West Africa.

**Special considerations for pregnancy and obstetrics**
Pregnant women with EVD are at increased risk of severe disease and death. Spontaneous abortion and uterine bleeding are common. Women may present in any trimester, and may or may not be in labour on presentation. The fetus, placenta and amniotic fluid are highly infectious, and remain so even if the mother survives and is PCR negative for ebola on blood testing. Pregnancy loss is common in all trimesters, and all liveborn neonates to date have died. Delivery is a major risk for
transmission of ebola to healthcare workers; several epidemics have started when a pregnant
women with undiagnosed ebola delivers, and birth attendants subsequently infected.

Management principles for pregnant women with ebola are as follows:

- Optimise maternal survival: maximal supportive medical management of the mother both of
  EVD and during delivery, particularly if complications such as postpartum haemorrhage occur.
- Maternal survival is the priority, given the dismal prognosis for the infant.
- Avoid surgical intervention. Surgical procedures such as caesarean section while wearing full PPE
  carries significant risks both for the mother and for health care workers, and should not be
  performed.
- If the mother survives and subsequently tests negative for ebola, the placenta, amniotic fluid
  and fetus remain highly infectious. Pregnant women must remain in a high-risk isolation unit
  until they have delivered, and be discharged only after delivery.

All women of reproductive age with EVD should have a pregnancy test.

See appendix for full discussion of the management of EVD in pregnancy.

Special considerations for paediatrics
Since children comprise a small percentage of EVD cases, detailed information about paediatric
cases has not been systematically collected. However, in two previous EVD outbreaks in which large
numbers of children were affected, school-aged children and adolescents had higher survival rates
compared with children younger than 5 years of age. Anecdotal experience during the current
outbreak in West Africa supports this finding.
Typically, children may present with nonspecific signs and symptoms of EVD similar to those in
adults. Malaria, measles, typhoid fever and other infectious diseases endemic in West Africa must be
included in the differential diagnosis. If, for any reason, malaria testing is delayed, empiric
antimalarial therapy is strongly recommended until malaria investigation results are available and
synchronous malaria infection confidently excluded.
Children are especially susceptible to electrolyte abnormalities and hypovolaemia, so aggressive
treatment and early recognition of complications is essential.
References


19. Gulland A. First Ebola treatment is approved by WHO BMJ 2014;349:g5539 doi: 10.1136/bmj.g5539 (Published 8 September 2014)


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Appendix: Ebola Virus Disease and Pregnancy

Pregnant women infected with ebola are at increased risk of severe disease and death. Spontaneous abortion and uterine bleeding are common. Women may present in any trimester, and may or may not be in labour on presentation. The fetus, placenta and amniotic fluid are highly infectious, and remain so even if the mother survives and is ebola PCR negative on blood testing. Pregnancy loss is common in all trimesters, and all liveborn neonates to date have died. Delivery is a major risk for transmission of ebola to healthcare workers; several epidemics have started with a pregnant woman with undiagnosed ebola delivering, and birth attendants subsequently infected. Pregnant health care workers should not care for patients with EVD.

The principles of management for pregnant women with ebola are as follows:

- Optimise maternal survival: maximal supportive medical management of the mother
- Maternal survival is the priority, given the dismal prognosis for the infant
- Avoid surgical intervention

Surgical intervention such as caesarean section while wearing full PPE carries significant risks both for the mother and for health care workers. EVD presents an extraordinary set of challenges and circumstances that may limit usual obstetric management. Consensus is that surgical procedures that would generally be performed for maternal benefit (caesarean section for obstructed labour, hysterectomy for ruptured uterus) should not be performed. They would be extraordinarily challenging, liable to result in serious surgical complications, and would carry a significant risk for the mother and for attending healthcare workers. Full supportive care should be given, and pain actively managed. See section on ethical considerations below.

Management of pregnant women with ebola virus disease consists of the following:

- Diagnosis of both pregnancy and ebola virus disease
- Management of ebola virus disease
- Management of the pregnancy

Diagnosis of pregnancy and of Ebola Virus Disease

All women of reproductive age with EVD should have a pregnancy test.
Pregnant women with uterine bleeding should be considered ebola suspects irrespective of the presence of fever or other symptoms. Pregnant women are generally admitted directly to a labour ward, and may bypass screening and isolation facilities in an emergency department. It is essential that midwives and obstetric doctors are alert for pregnant women who are within 21 days of leaving an ebola-affected country, and any potential contact with anyone with confirmed or suspected ebola. Travel history is routinely taken for all women admitted to a labour ward; followed by symptom screening (PV bleeding, fever, vomiting and diarrhoea). PV bleeding may be the only symptom, and therefore the travel history, and if there has been any possible contact with a patient with ebola is of utmost importance. Many obstetric or medical conditions in pregnancy may have similar presentations to EVD; these include malaria, bacterial sepsis, pre-eclampsia/HELLP syndrome and TTP. Senior obstetricians must be involved, and liaise with Infectious Diseases Specialists. The pregnant woman should be isolated and intervention avoided until the ebola PCR result is available. Pregnant women where suspicion is high for EVD should be transferred to the nearest high level isolation unit, and not remain on the labour ward.

Management of Ebola Virus Disease
Mortality in pregnant women is as high as 95%. Supportive management must therefore be optimal, to maximise maternal survival. Intravenous access should be established on admission.

Blood and blood products should be given early and pro-actively for obstetric or non-obstetric related haemorrhage. A target haemoglobin of > 10g/dL is recommended for pregnant women, and platelet count >50 x 10^9/L for pregnant women in labour, with antepartum or postpartum haemorrhage, or bleeding due to other causes. If INR >2, fresh frozen plasma (FFP) should be given, and if the fibrinogen level is low in the face of significant haemorrhage, cryoprecipitate should be transfused.

Management of Pregnancy
Pregnant women may present in any trimester. Intra-uterine fetal death is common at presentation; the woman should be asked if she is still feeling fetal movements. The majority of pregnant women go into spontaneous labour irrespective of trimester, and may be in labour on admission.

Management of delivery is expectant. Fetal monitoring is not indicated; intervention for fetal reasons is not indicated.
Maintaining good infection control is of utmost importance during delivery. Health care workers should stand to the side of the patient, and not in front, where they are at risk of splashes from blood and amniotic fluid. Gloved hands should be washed in chlorine between all contact with the patient, fetus and blood/amniotic fluid.

Ideally, there should be 4 experienced healthcare workers in attendance:

- 2 to manage the delivery
- 1 to manage IV fluids and drugs, and to estimate blood loss
- 1 to ensure infection control procedures and strictly observed, and to clean any splashes or spills of body fluids

Vaginal examinations should be minimised, and sterile procedures observed to minimise the risk of postpartum sepsis. All invasive procedures should be avoided, including artificial rupture of the membranes, uterine evacuation, manual removal of placenta, episiotomy, and assisted delivery with forceps or vacuum. Opiate analgesia can be given for pain management.

**After delivery**

Syntometrine should be given intravenously after delivery of the baby, to prevent postpartum haemorrhage. If the infant is alive, the cord should be clamped and divided, and the baby given to the mother. Neonatal resuscitation will not be performed. The baby should be considered infected, and should only be handled by healthcare workers in full PPE. Experience to date is that liveborn infants do not survive. The baby can therefore be breastfed if the mother’s condition allows, otherwise formula should be given. If the mother is not breastfeeding, cabergoline 1mg should be given to suppress lactation. If the baby is stillborn, the cord need not be clamped and cut.

**Delivery of the placenta**

This should be expectant; and controlled cord traction not performed. Oral misoprostol 200 micrograms 2 hourly should be given if the placenta fails to separate, or if there is haemorrhage before or after delivery of the placenta.

**Management of postpartum haemorrhage**

Ongoing postpartum haemorrhage should be managed with oxytocin, misoprostol and intravenous fluids. Blood and blood products should be given to replace blood loss and correct coagulopathy.
Retained products of conception, retained placenta
Avoid any invasive procedures, such as manual removal or curettage. Misoprostol should be given orally or rectally, and expulsion of placental tissue awaited. Even if this takes days rather than hours, expectant management should continue. Antibiotic cover should be given, with a cephalosporin (likely started on admission), and metronidazole. Sepsis of genital tract origin should be treated with antibiotics, and surgical intervention avoided.

Disposal of fetus and placenta
These are highly infectious. They should be placed on an absorbable cloth, sprayed with chlorine, wrapped in more absorbable cloth, sprayed again and wrapped in a child body bag.

If the mother survives, and is undelivered
If the mother survives and tests negative for ebola, the placenta, amniotic fluid and fetus remain highly infectious. Pregnant women should therefore deliver in a high-risk isolation unit, and only be discharged after delivery.

Intra-uterine death is common, and may have already occurred; induction of labour with misoprostol is therefore indicated. If the fetus is still alive, there are 2 management options. The first is expectant management, while remaining in the high risk isolation unit; the second is termination of pregnancy/induction of labour depending on gestation. Experience has shown that induction of labour with misoprostol is safe for pregnant women during the recovery phase of EVD.

Palliation
If a pregnant or delivered woman is moribund because of uncorrectable haemorrhage, sepsis or obstructed labour, she should be palliated with narcotic analgesia.

Ethical considerations
These guidelines will apply in general. Specific cases may merit some deviation from this guideline. This would need to follow deliberate discussion and explicit agreement about the nature of the deviation and the risks that may arise. These issues will need to be considered by all members of the health care team (doctors, nursing staff, managers etc) before any such action can be endorsed.

Where doubt arises about the management of individual cases, ethical consultation is to be considered.
References


Black, BO. Obstetrics in the time of Ebola: challenges and dilemmas in providing lifesaving care during a deadly epidemic. BJOB 2015;122: 284-86.

W Cape provincial policy statement. Obstetric management of ebola infected pregnant women. (draft).