



GLOBAL TASK FORCE ON CHOLERA CONTROL

Interim Technical Note

Treatment of cholera in pregnant women

30 September 2020

The link between cholera in pregnancy and negative childbirth outcomes has been observed since the 19th century, but there is currently no clear understanding of the extent nor the mechanisms to inform treatment guidelines. The recommendations in this Interim Technical Note are based on current knowledge, including documented experiences of treating pregnant women with cholera during epidemics.

There is no evidence that pregnant women, at any stage of pregnancy, are at greater risk of being infected with *Vibrio cholerae* than the general population.

The symptoms and complications of cholera for a pregnant woman are the same as for other patients (e.g. mild to severe dehydration, hypovolaemic shock), however, there is an additional risk of foetal complications including spontaneous abortion, pre-term labour and intra-uterine foetal death. Although data is limited, results of a meta-analysis published in 2015 show that in pooled data from 1991-2013, foetal death rates associated with symptomatic maternal cholera were 7.9% (95% CI 5.3-10.4) with a pooled relative risk as compared to national data of 3.8 (95% CI 2.1-7.0). No difference in risk of foetal death by trimester was seen. The same analysis reports no statistically significant increase in the risk of maternal death.¹

Currently there is little evidence on the pathways causing these complications, but severe dehydration due to cholera or other diarrhoeal diseases in pregnant women have been identified as risk factors.

The following treatment recommendations are based on current knowledge and best practices to maintain or correct maternal and therefore foetal hydration.

This Interim Technical Note is designed to help clinical teams working in a cholera treatment structure provide the best care possible for pregnant women. Any woman with severe complications of pregnancy, not linked to cholera, including severe pre-eclampsia and ante-partum hemorrhage should be rapidly transferred to an obstetrical centre for more specialised care. The woman should be isolated from other patients and strict infection prevention and control (IPC) measures implemented to ensure no other women in the obstetrical centre are infected with cholera.

¹ Tran N-T, Taylor R, Anierens A, Staderini, N (2015) Cholera in pregnancy: a systematic review and meta-analysis of fetal, neonatal and maternal mortality PLoS One 10(7):e0132920. Doi:10.1371/journal.pone.0132920.

Assessing and treating a pregnant woman with cholera

a. Clinical evaluation

First trimester: initial evaluation is the same as for the general population of adults with suspected cholera.

Second and third trimester: place the woman in the supine position on her left side (left lateral position) and use standard criteria to determine the degree of dehydration (see Table 1 below). Women in 2nd and 3rd trimester have increased blood volume which may make it more difficult to see signs of dehydration.

Perform the skin pinch under the clavicles rather than the gravid abdomen.

In addition, measure systolic blood pressure, it should be between 90 and 120 mmHg.

Measure capillary blood glucose (if glucometer is available) and body weight, whenever possible [on admission or as soon as the patient can stand or sit (if sitting weighing scale is available) safely.

Note: Avoid positioning the patient on her back: as pregnancy progresses, the increasing weight and positional rotation of the uterus will compress the inferior vena cava reducing blood flow to the heart thereby decreasing cardiac output.

Table 1: Signs of dehydration

Degree of dehydration	Signs
Severe dehydration (Plan C)	One or more danger signs: <ul style="list-style-type: none">• Lethargic or unconscious• Absent or weak pulse AND/OR <ul style="list-style-type: none">• Systolic blood pressure <90 mmHg AND/OR <ul style="list-style-type: none">Any two signs of severe dehydration:<ul style="list-style-type: none">• Sunken eyes (recent change)• Skin pinch under clavicle goes back very slowly (> 2 seconds)• Not able to drink or drinks poorly• Foetal heartrate above 160 beats per minute
Some signs of dehydration (Plan B)	No danger signs, systolic blood pressure > 90 mmHg AND at least 2 of the following: <ul style="list-style-type: none">• Irritable or restless• Sunken eyes (recent change)• Rapid pulse (above 100 beats per minute)• Thirsty (drinks eagerly)• Sink pinch under clavicle goes back slowly (< 2 seconds)

	<ul style="list-style-type: none"> • Foetal heartrate above 160 beats per minute.
No signs of dehydration (Plan A)	<ul style="list-style-type: none"> • Awake and alert • Normal pulse • Normal thirst • Eyes not sunken • Skin pinch under clavicle normal [disappears immediately] • Foetal heart rate normal (110-160 beats per minute)

b. Treatment

The objectives of treatment are to:

- Prevent or correct maternal dehydration
- Protect the foetus by maintaining systolic blood pressure above 90 mmHg to ensure adequate uterine blood flow
- Protect the foetus by maintaining adequate glucose levels in the mother

Table 2: Treatment for cholera for pregnant women

Trimester	Level of assessed dehydration	XXX	Antibiotic treatment All pregnant women should receive antibiotics
First trimester	All	Follow standard treatment protocols for rehydration.	First line (if local strain sensitive): Doxycycline 300 mg p.o. single dose Alternatives: Azithromycin 1 g p.o single dose or ciprofloxacin: 1 g p.o. single dose.
Second and third trimester	Any danger sign or systolic blood pressure < 90 mmHg or severe dehydration (Plan C)	Immediate: Bolus of 30 ml/kg of Ringer's Lactate over 30 minutes Repeat the bolus if: – the pulse remains weak, or – systolic blood pressure remains ≤ 90, or – consciousness remains altered – any additional danger sign was present and has not resolved • Once the patient has stabilized: Continue with 70 ml/kg of Ringer's Lactate over 3-4 hours AND If little or no vomiting: – approximately 250 ml of ORS	First line (if local strain sensitive): Doxycycline 300 mg p.o. single dose Alternatives: Azithromycin 1 g p.o single dose or ciprofloxacin: 1 g p.o. single dose

		<p>after each stool.</p> <p>If the patient is vomiting frequently (≥ 3 per hour) or is otherwise unable to retain ORS, on-going fluid losses can be replaced via the IV route (add at least 250 ml of Ringer's Lactate for each stool).</p>	
Signs of some dehydration (Plan B)	<p>Oral rehydration: 75 ml/kg ORS over 4 hours + approximately 250 ml of ORS after each stool</p> <p>If the patient has difficulty drinking ORS, or is vomiting frequently (≥ 3 per hour) pass rapidly to IV rehydration (75 ml/kg of Ringer's Lactate).</p> <p>If the systolic blood pressure drops below < 90 mmHg or any danger signs or signs of severe dehydration appear, switch to treatment for severe dehydration.</p>	<p>First line (if local strain sensitive): Doxycycline 300 mg p.o. single dose</p> <p>Alternatives: Azithromycin 1 g p.o single dose or ciprofloxacin: 1 g p.o. single dose</p>	
No signs of dehydration (Plan A)	<p>Plan A</p> <p>Approximately 250 ml of ORS after each stool</p> <p>If the patient is vomiting frequently or is having trouble drinking sufficient ORS, switch to IV route.</p>	<p>First line (if local strain sensitive): Doxycycline 300 mg p.o. single dose</p> <p>Alternatives: Azithromycin 1 g p.o single dose or ciprofloxacin: 1 g p.o. single dose</p>	

i. Monitoring patients with severe dehydration or danger signs

During the initial bolus period

- Observe closely until a strong radial pulse is present and mental status improves.
- Check the volume of fluid infused.
- Ensure that the infusion rate is sufficient to administer the prescribed quantity within the correct time frame and that the IV cannula is not blocked.
- Record the amount of fluid given.
- If there is no improvement with the first bolus or if at any time the systolic blood pressure falls ≤ 90 or danger signs reappear, administer a second bolus

Note: if the patient does not improve after two fluid boluses, check for hypoglycaemia.

Measure blood glucose and treat accordingly, if no glucometer is available, administer glucose empirically (see section Hypoglycaemia below).

During the next 3 hours

- Assess at least every 30 minutes, monitoring should include:
 - Maternal respiratory rate and blood pressure
 - Foetal heart rate
- Ensure that the infusion rate is sufficient to administer the prescribed quantity within the correct time frame and that the IV cannula is not blocked.
- As soon as the patient is able, start to give ORS in addition to the IV infusion.
- Note the amount of fluid given (Ringer's Lactate and ORS).

- Note the number of stools and vomiting episodes (mark a cross for each stool or vomiting) and ensure the patient takes 250 ml of ORS for each stool or vomiting episode to correct for ongoing losses.
- Closely monitor patients with profuse diarrhoea and vomiting.

- Keep monitoring for danger signs, if the systolic blood pressure falls ≤ 90 or danger signs reappear, repeat fluid bolus until the danger signs improve, and then continue prior fluid therapy. As above, closely monitor maternal respiratory rate and blood pressure for signs of fluid overload and foetal heart rate for signs of distress.

If the patient is vomiting frequently (≥ 3 per hour) or is otherwise unable to retain ORS, on-going fluid losses can be replaced via the IV route (add at least 250 ml of Ringer's Lactate for each stool).

Reassess at the end of the IV rehydration phase

After the prescribed amount of Ringer's Lactate has been given, reassess the hydration status; if there are no signs of dehydration, the patient can then switch to treatment plan A. Stop the infusion but leave the IV cannula in place.

However, if a patient was more dehydrated than initially assessed or if on-going losses have not been fully replaced, some signs of dehydration may still be present at this point.

- If signs of severe dehydration are still present, repeat the 3-hour IV rehydration treatment, including another bolus.
- If some signs of dehydration are present, continue the rehydration phase with 75 ml/kg of ORS over 4 hours (standard plan B). Stop the infusion but leave the IV cannula in place. In these patients, continue the clinical evaluation hourly until the signs of dehydration have resolved and the patient can switch to treatment Plan A, giving as much ORS as wanted after each loose stool.

ii. *Standard monitoring for patients with some or no signs of dehydration*

- Check maternal systolic blood pressure, heart rate and respiratory rate and foetal heart rate every 30 minutes.
- Check signs of dehydration every hour to see if the patient is improving.
- Note the amount of ORS given and ensure it is as much as is prescribed and is also making up for ongoing losses.
- Note the number of stools and vomiting episodes (mark a cross for each stool or vomiting).
- Check patients with frequent diarrhoea and vomiting more frequently.

- If the systolic blood pressure is ≤ 90 or signs of severe dehydration appear, start IV therapy for severe dehydration.
- If the woman is thirsty and wants to drink more than prescribed, give more Oral Rehydration Solution (ORS).

iii. *Monitor all patients for hypoglycaemia*

There is no evidence that systematically adding glucose or potassium to rehydration fluid is beneficial for the foetus.

If the mother presents with clinical signs of hypoglycaemia or hypokalaemia, then appropriate therapy should be given.

To prevent hypoglycaemia, give ORS therapy as soon as possible to all patients receiving IV treatment and start giving normal food as soon as possible.

Clinical signs of hypoglycaemia

- Decreased levels of consciousness or hypotonia persist after 2 boluses of Ringer's Lactate.
- Neurologic signs (lethargy or coma) appear when signs of dehydration are resolving during rehydration therapy.
- Hypothermia

A blood glucose level < 60 mg/dl (< 4 mmol/litre) indicates hypoglycaemia.

Treatment of hypoglycaemia

- Administer glucose by slow IV injection:
 - Adults: 5ml/kg of 10% glucose or equivalent.
- Reassess glucose level after 30 minutes and repeat the same dose if necessary.
- To prevent relapse, give ORS under observation. If ORS consumption is delayed or reduced: add 100 ml of 50% glucose per litre of Ringer's Lactate/ Cholera Saline to be used for rehydration (making a 5% glucose solution) until sufficient ORS intake is possible.

Transferring a pregnant woman with cholera to a maternity ward

If any signs or symptoms appear that threaten the life of the mother, including eclampsia, post-partum haemorrhage or pre-term labour (less than 34 weeks) transfer to a maternity ward. Try to stabilize the patient haemodynamically with Ringer's Lactate infusion, to get the systolic blood pressure > 90 , before transfer.

For other complications including spontaneous abortion (if there is no significant, persistent bleeding) or intra-uterine death, try to complete treatment for cholera in the CTC and transfer to a maternity ward on discharge from the CTC.

If the woman goes into pre-term labour and the cervix is closed, the contractions will likely stop as cholera resolves. If contractions persist after rehydration is completed, transfer to a maternity unit for possible treatment of premature labour. Tocolytics are not part of the basic cholera pharmacy, but should be considered if available.

Births in a treatment centre

If transfer of the woman is not possible or delivery happens too quickly for transfer, follow local obstetric recommendations.

Provide as much privacy as possible for the woman during delivery and ensure respectful maternity care is provided

If the baby is delivered before 32 weeks gestation or weight is less than 1500g at birth, transfer immediately to hospital. Keep the baby warm during transfer and encourage breast feeding.

Following delivery, assess both mother and baby.

If any danger signs are present, refer as quickly as possible to hospital. The hospital should be made aware that the mother was being treated for cholera so that they can ensure adequate IPC measures.

Danger signs for the baby include:

- Fast breathing (more than 60 breaths per minute)
- Slow breathing (less than 30 breaths per minute) or gasping or grunting
- Severe chest in-drawing
- Heart rate constantly above 180 beats per minute
- Fits or convulsions
- Floppy or stiff or no spontaneous movement
- Jaundice or cyanosis
- Temperature below 35.5°C (and unable to warm) or above 37.5°C
- Bleeding from umbilical stump or umbilicus draining pus or swelling

Danger signs for the mother include:

- Heavy vaginal bleeding (more than 1 pad soaked in 5 minutes)
- Uterus not hard and round
- Temperature greater than 38°C and any of the following: chills, foul-smelling vaginal discharge, low abdominal pains
- Perineal tear extending to anus or rectum

For further information on maternal and newborn care refer to: World Health Organization (2015), Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice -3rd edition (https://www.who.int/maternal_child_adolescent/documents/imca-essential-practice-guide/en/)

Care for a neonate in a Cholera Treatment Centre

If a baby is born in the Cholera Treatment Centre (CTC) and at any time the neonate comes into contact with faeces, wash with soap and water. Do not use a chlorine solution or other antiseptic solution.

Mothers should be encouraged to breast feed. The mother should be encouraged to wash her hands with soap and water before putting the neonate to breast.

Administration of antibiotic prophylaxis to the neonate for prevention of cholera is not necessary.

Note: If there is a reason to believe that the mother's breast has been in contact with stool or vomit, consider asking the mother to clean her breast with soap and water and expressing some small amount

of breast milk on her nipple and areola before putting the neonate to feed. Do not use chlorine or other antiseptic solutions. There is insufficient available evidence to make a strong recommendation, however breastfeeding should always be encouraged. Institution of any barriers to breastfeeding should be evidence based and, on a case-by-case basis.

Referral for care following discharge from the Cholera Treatment Centre

If a baby is born in the CTC, at discharge from the CTC, refer the mother and neonate for post-natal consultation.

All pregnant women and any women who have had a stillbirth/spontaneous abortion or who have delivered a baby in the CTC should be referred to antenatal care or to continue ante-natal care if they were already enrolled, when discharged from treatment in the CTC.

References

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