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EDITORIAL

Severe Acute Respiratory Syndrome and pregnancy

Severe Acute Respiratory Syndrome (SARS) has already had an enormous impact on society and medical practice but presents special problems in pregnancy. The following comments are based on the experience of those in Hong Kong caring for patients with SARS in pregnancy of which there have been 10 at the time of writing in May 2003.

The disease causes atypical pneumonia and some patients rapidly progress to adult respiratory distress syndrome. This results in significant hypoxia. It may be associated with miscarriage in early pregnancy (as occurred in four of the five Hong Kong patients admitted in early pregnancy), fetal distress, intrauterine growth restriction and intrauterine death. To minimise these fetal effects, attempts should be made to keep the maternal arterial saturation above 95%. If there is maternal desaturation, patients have to sit upright because of respiratory distress. Once patients require mechanical ventilation, they should lie on their left sides to maximise maternal uterine blood flow. The fetus should be monitored with cardiotocography and ultrasound for growth and Doppler blood flow studies.

SARS may also lead to renal failure, disseminated intravascular coagulation and multi-organ failure. Maternal critical illness may lead to premature rupture of membranes or premature labour. Tepid sponging has been advocated to lower maternal pyrexia and the risk of preterm labour.

SARS is a very contagious viral infection, transmitted through droplets and close contact. Health care workers are particularly at risk and must take appropriate infection control precautions. Pregnant women with SARS must be isolated from other antenatal and postnatal patients. Precautions against airborne infection such as using a N95 mask (equivalent or higher standard, i.e. N100) should be practised in the whole SARS ward. The viral load is sufficiently high to cause contamination. To avoid cross infection of other team members and antenatal patients, a small group of health care attendants should be designated to handle these patients. This group should be regularly monitored for symptoms and signs of infection. The risk of cross infection is particularly high at the time of vaginal or operative deliveries, especially when there is maternal viraemia. Additional protection against airborne cross infection is needed, using negative pressure air circulation.

Because of the risk of additional bacterial infection, broad-spectrum antibiotics have been recommended for treatment (in pregnancy clarithromycin 500 mg twice daily plus coamoxiclav 375 mg thrice daily)[1].

Ribavarin has been advocated as an antiviral agent for patients who are very sick and/or rapidly deteriorating even though there is no good evidence of its efficacy in SARS. However, there are concerns about its use in early pregnancy. Ribavarin has caused limb reduction deformities when given to hamsters in a single dose of 2.5 mg/kg, on a weight basis one tenth of the 2400 mg daily dose recommended[1] for humans with SARS. There are no human data for early pregnancy use. There have not been any fetal problems reported in the very few women given ribavarin in the second half of pregnancy[2,3]. If it is thought necessary to give ribavarin during embryogenesis, women should be counselled about the advisability of termination of pregnancy.

High dose steroids starting with pulsed methylprednisolone and tapering to low doses of oral prednisolone have also been advocated[1]. Any possible adverse effect of this regime on the fetus might seem small by comparison to the potential maternal benefit. However, in the Hong Kong series, two deaths were in association with multidrug resistant *Staphylococcus aureus* (MRSA) septicaemia in women who had received high dose steroids. One death was due to progressive respiratory failure — ARDS, but the other was due to septicaemic shock. The resultant immune suppression from high dose steroids must be considered a factor. Even if the woman has been given high dose prednisolone, additional dexamethasone should be given if she is being delivered preterm because of the inadequate placental transfer of prednisolone. Extra steroid may be necessary at the time of delivery to prevent maternal Addisonian collapse.

SARS is most likely to be due to a new coronavirus similar to those that cause influenza. Pregnant women appear to be particularly susceptible to epidemic viral pneumonia. For example, in New York, at the time of the Asian influenza epidemic of 1957, half of the maternal deaths were due to pneumonia[4]. In addition, varicella pneumonia seems to be more common in pregnancy and to have a worse prognosis with higher mortality than in the non-pregnant state. Our own experience with SARS in Hong Kong is in keeping with the extra risk of pregnancy in viral illness. In the seven cases of SARS in pregnancy admitted to the Princess Margaret Hospital (the designated hospital for all pregnant SARS cases), two (28%) have died and four (57%) have been admitted to intensive care for assisted ventilation by contrast with mortality rates of 10% and ICU admission rates of 20% in the non-pregnant population.

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Therefore, it is tempting to recommend early delivery or termination of pregnancy in pregnant women who are seriously ill with SARS. If pregnancy makes SARS worse, then no longer being pregnant might make it better whatever the mechanism for the poorer outcome in pregnancy. More importantly, in the second half of pregnancy, removal of the feto-placental unit will reduce oxygen consumption about 50 mL per minute and this could be critical in a woman in severe respiratory failure. Criteria that have been considered for early delivery include:

1. Maternal rapid deterioration
2. Failure to maintain adequate blood oxygenation
3. Difficulty with mechanical ventilation due to the gravid uterus
4. Multi-organ failure
5. Fetal compromise
6. Other obstetric indications

In the patient who is ventilated but not critically ill, there is a case for delivery once fetal maturity is reasonably secure, say at 34 weeks. Delivery can be performed electively, there are more treatment options available should she deteriorate unexpectedly and management of the ventilated patient is simpler if she is not pregnant. Such decisions must be made in discussion with the patient or her family emphasising our current lack of firm evidence.

At present there seems to be no reason for elective preterm delivery of the woman who is relatively well with SARS. In particular, there is no evidence that early delivery will reduce the risk of materno-fetal transmission of the virus, a risk that is currently only theoretical. Indeed, early delivery probably puts the baby at higher risk of exposure to the SARS-associated coronavirus. None of the babies born in Hong Kong have shown evidence of infection on the basis of PCR studies. The final answer will come in about six months when they can be tested for antibody status.

Ideally, these patients should be delivered vaginally with epidural block if possible. Concern has arisen that regional block might increase the risk of maternal central nervous system infection. However, PCR studies performed on spinal fluid obtained at the time of spinal block have shown that the spinal fluid already contains SARS-associated coronavirus, presumably having crossed the blood–brain barrier before the procedure.

If the women are very sick and/or remote from term, caesarean section is likely to be necessary. Women who are already being ventilated will be delivered with general anaesthesia. Those who have severe respiratory involvement without being ventilated would be better managed with elective general anaesthesia rather than with epidural block, which runs the risk of needing emergency ventilation during the procedure as a consequence of involvement of the costal muscles.

Managing patients in convalescence also causes problems. We do not know the risk of fetal infection or likelihood of viral excretion by the newborns. Infection control measures should be undertaken to protect the medical and nursing staff handling these cases. After delivery, babies are being nursed in isolation until they are judged to be free of virus by clinical and laboratory criteria. By analogy with HIV infection, women are advised not to breast feed until more is known about the secretion of the coronavirus in breast milk. Ribavarin has a long half-life. Those who have taken it should use effective contraception for at least six months before becoming pregnant.

This review has shown that there are many uncertainties about the interaction between SARS and pregnancy. Hopefully, some of these will be resolved as knowledge increases and the natural history of the condition becomes clearer.

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