APPENDIX.

Antenatal and obstetric care

In Hong Kong, public antenatal and obstetric care is jointly shared between government's Maternal and Child Health Centres (www.fhs.gov.hk) and the hospital obstetric units under the Hospital Authority (www.ha.org.hk). The Maternal and Child Health Centres are responsible for routine antenatal follow-up of low-risk cases beginning in the first trimester; the follow-up is performed every 4 weeks until 32 weeks, every 2 weeks until 37 weeks, and then weekly until delivery. During each visit in Maternal and Child Health Centres, basic examinations are performed (eg, symphyseal-fundal height measurement, foetal presentation, blood pressure, and urinalysis). Foetal movement is determined by clinical interviews; the foetal heart rate is checked by Doptone in each visit. Hospital obstetric units under the Hospital Authority (including the study unit) are responsible for follow-up of high-risk cases, as well as childbirth. Antenatal and obstetric care are performed in accordance with Hong Kong College of Obstetricians and Gynaecologists guidelines. During the study period, Down syndrome screening using a second trimester biochemical test was provided for women with advanced maternal age before 2009; beginning in 2010, this was included in universal first trimester combined screening.[1] Women could also attend private clinics for non-invasive prenatal testing with cell-free DNA for more accurate results; public non-invasive prenatal testing was launched in late 2019 for patients who were considered high-risk because of first trimester combined screening results. During the study period, other routine blood tests screened for thalassaemia, blood group, human immunodeficiency virus, syphilis, hepatitis B, and rubella. Foetal morphology scanning is not routine; during the study period, it was performed for high-risk cases.[2] However, women often attended private clinics for morphology scanning. Oral glucose tolerance tests were arranged for high-risk individuals (eg, patients with maternal obesity, advanced maternal age, and/or family history of diabetes). Universal group B streptococcal screening was implemented in 2012.[3,4] Throughout the study period, labour induction was routinely performed at 41 to 42 weeks.[5-7] Universal continuous intrapartum foetal monitoring with cardiotocogram was implemented except in unusual situations, such as lethal foetal anomalies (eg, Haemoglobin Barts diseases, anencephaly, trisomy 13, or trisomy 18) or borderline viability in which parents decided not to undergo emergency caesarean section because of risk to the foetus.

Protocol for investigation of stillbirth and neonatal death

The study unit had a standard protocol for investigating causes of stillbirth and neonatal deaths. A perinatal meeting was conducted each month to review all cases of stillbirth and neonatal death to confirm the underlying causes. Stillbirth was diagnosed based on the absence of foetal heart pulsation with ultrasonic confirmation by trained obstetricians; it was also diagnosed in cases where signs of life were absent at birth or maceration was present at birth. When stillbirth was diagnosed, detailed history collection, physical examination, and investigations were performed to identify cases that had involved obstetric emergencies requiring patient stabilisation and prompt delivery. Workup was then performed to detect underlying causes that may have led to foetal death. Maternal blood was subjected to multiple tests (eg, haemoglobin A1c, thyroid function, autoimmune markers, and bile acid) to rule out underlying medical conditions. The Kleihauer test was performed before delivery to rule out foetal maternal haemorrhage. The TORCH (toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex) screening protocol was performed to detect congenital infection. Bacterial cultures were used to analyse mid-stream urine, high vaginal secretions, and placentas to identify any infectious components. Placentas were subjected to histopathological examination and karyotyping. Viral swabs were collected from the bodies of stillborn babies, then subjected to post-mortem examination. The times of all major events were clearly documented in medical records.

Foetal growth restriction (FGR) was diagnosed in cases with an antenatal ultrasound that showed foetal abdominal circumference or estimated foetal weight below the third centile, or below the tenth centile in combination with other abnormalities (eg, oligohydramnios or abnormal pulsatility indexes). However, FGR in some foetuses was not detected before birth; therefore, we also included foetuses with birthweight below the third centile as FGR. Placental pathology was confirmed by histopathological assessments. Chorioamnionitis was defined as 'acute chorionitis, villitis, and funisitis' on histopathological analysis of placenta; this finding was combined with positive maternal culture result, positive foetal viral swab, or documented intrapartum maternal pyrexia with elevated inflammatory markers.

While a stillbirth might have multiple pathologies or risk factors, we selected only one factor for each pregnancy as the leading cause

of stillbirth. The ranking system for determining the leading cause was based on a combination of clinical judgement and laboratory results. First, we prioritised lethal congenital malformations or genetic disorders, as well as emergencies (eg, cord prolapse, uterine rupture, or placental abruption). For example, if a case involved pre-eclampsia complicated by placental abruption, placental abruption was regarded as the leading cause. If foetal Haemoglobin Barts disease was complicated by pre-eclampsia, Haemoglobin Barts was considered the leading cause. Next, we prioritised pre-eclampsia, medical diseases, and placental pathologies which might be associated with FGR. Foetal growth restriction was considered the leading cause only when these underlying causes were absent. Panel discussions were conducted regarding cases in which causes were difficult to determine/categorise. The classification was 'unexplained stillbirth' if all known causes were ruled out.

Antenatal stillbirth was defined as any foetal death that occurred before the onset of labour. Intrapartum stillbirth was defined as any foetal death that occurred during labour; it also included any foetal death related to placental abruption, uterine rupture, cord prolapse, in which the onset of labour was not well-defined but emergency delivery was required.

References

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