Clinical Guideline

Investigation of Stillbirths: SA protocol

Policy developed by: SA Maternal & Neonatal Community of Practice
Approved SA Health Safety & Quality Strategic Governance Committee on:
19 April 2016
Next review due: 19 April 2019

Summary
Clinical practice guideline on the investigation of stillbirths in South Australia.

Keywords
clinical guideline, investigation of stillbirths in south australia, investigation, stillbirth, full blood examination, kleihauer, psanz, fluorescence-activated cell sorting, facs, autopsy, external examination, histopathology, placenta, state perinatal autopsy service, guthrie card, congenital abnormality, vasculopathies, placental abruption, fetal growth restriction, pre-eclampsia, intrauterine growth restriction, intrapartum stillbirths, unexplained stillbirths

Policy history
Is this a new policy? N
Does this policy amend or update an existing policy? Y v1.0
Does this policy replace an existing policy? N
If so, which policies?

Applies to
All SA Health Portfolio

Staff impact
All Staff, Management, Admin, Students, Volunteers
All Clinical, Medical, Nursing, Allied Health, Emergency, Dental, Mental Health, Pathology

PDS reference
CG235

Version control and change history

<table>
<thead>
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Note

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient’s medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:
The aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant women. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that Perinatal services prepare to respectively manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.
Stillbirth investigations algorithm

CORE INVESTIGATIONS OF ALL STILLBIRTHS

AT DIAGNOSIS OF FETAL DEATH

Maternal History
- Take full Maternal History

Blood Tests
- Full Blood Examination and smear for nucleated red cell count
- Group & antibody screen
- Kell
- Renal Function Tests including Urate
- Liver Function Tests including Bile Acid
- Thyroid Function Tests
- HbA1c
- Cytomegalovirus, Toxoplasma and Parvovirus B19 serology
- Rubella & syphilis serology if not already done antenatally
- Thrombophilia Tests
  - Anticardiolipin antibodies
  - Lupus anticoagulant
  - APC Resistance
  - see further investigations following birth

Ultrasound Scan
- Fetal abnormalities
- Amniotic Fluid Volume

Amniocentesis
- Microbiological cultures
- Chromosomal analysis

Low vaginal/perianal culture

FOLLOWING BIRTH

Baby
- External examination
- Photographs
- Surface swabs
- Post-mortem examination

Cord / Cardiac Blood Samples
- Full Blood examination
- Chromosomal analysis
- Routine Guthrie test

Placenta & Cord
- Macroscopic examination of pia cerebral and cord
- Microbiological Cultures
- Biopsy for chromosomal analysis
- Placental histopathology

FURTHER INVESTIGATIONS BASED ON SPECIFIC CONDITIONS

*Positive Thrombophilia tests
- Fetal Growth Restriction
- Pre-eclampsia
- Placental vasculopathy/thrombosis
- Maternal/family thrombosis history
- Unexplained fetal death

Thrombophilia Studies 8-12 weeks postpartum
- Anticardiolipin antibodies
- Lupus anticoagulant
- APC Resistance
- Fasting Homocysteine
- Protein C & S deficiency
- Prothrombin Gene Mutation 20210A
- Anti-thrombin III

- if positive at birth
- Repeat
- Repeat
- Factor V Leiden Mutation
- MTHFR3 Gene Mutation

NB: Additional thrombophilia tests may be performed at birth where the above specific conditions or fetal growth restriction are known. MTHFR mutation testing should be performed when the following fetal anomalies are identified - cleft lip/palate, neural tube defects or congenital cardiac defects.

Introduction

> About 75% of the overall perinatal mortality in South Australia is related to stillbirths. Over the past several years approximately 11% of stillbirths had no cause identified, possibly, in part due to the lack of a systematic and up-to-date approach to the investigation of stillbirths for which there is no immediate obvious cause. Currently protocols for investigating such cases vary markedly between hospitals and generally have not kept pace with advances in obstetric knowledge, particularly in the area of vasculopathy.

> The ‘Stillbirth investigations algorithm’ of the Perinatal Society of Australia and New Zealand (PSANZ) above summarises the recommended core investigations for all stillbirths, and further investigations to be undertaken based on specific conditions.

> It is important that clinicians initiate a comprehensive approach to all cases of stillbirth; however, as in all aspects of clinical medicine common sense should prevail. In order to adequately assess causative and contributing factors in cases of stillbirth, certain core investigations will be required in all cases, as outlined in the ‘Core Investigations of All Stillbirths’ section in the ‘Stillbirth investigations algorithm’ above. South Australian specific considerations are summarised below. Some investigations are best suited to those cases in which no cause of death is apparent.

Aboriginal women should be consulted about any decisions in the first instance.

Aboriginal people experience very high levels of Grief and Loss in their communities. Stillbirth demands ceremonial acknowledgement Discuss with the Aboriginal Health Professional

South Australian core investigations (to be performed in all cases of stillbirth):

> The following outlines the current South Australian recommended core investigations into stillbirth.

> A detailed history and examination of the mother and careful review of the antenatal record can often provide clues to intercurrent infection, previously undiagnosed pre-eclampsia, drug use, obstetric cholestasis or missed intrauterine growth restriction.

> Maternal blood. In addition to the blood tests listed in the core investigations section of the ‘Stillbirth investigation algorithm’, a blood glucose test should be done. Testing for fetomaternal haemorrhage involves a Kleihauer test at SA Pathology and, if positive, Fluorescence-Activated Cell Sorting (FACS, a type of flow cytometry) to quantify the fetomaternal haemorrhage.

> Autopsy of the stillbirth. With parental consent, autopsy should be conducted by the State Perinatal Autopsy Service. In those cases where parents give full consent with regard to autopsy, the perinatal pathologists will take appropriate samples for genetic testing, and there is no need for the obstetrician to take separate fetal samples.

> External examination of the baby. In cases where parental consent for autopsy cannot be obtained, where possible, external examination of the baby by a pathologist experienced in this area should be sought. If this is not possible an X-ray of the baby and/or a clinical photograph should be taken and sent to a major centre for review.

> Histopathology of placenta. Whether or not an autopsy is performed the placenta should be placed in a dry sterile container (no formalin or saline), the container surrounded in ice and forwarded to the State Perinatal Autopsy Service. Histopathological examination combined with other investigations may provide a diagnosis and information that can be helpful in planning another pregnancy.
Guthrie card. Where permission for an autopsy has been declined, parents should be asked if blood can be taken for the Newborn Screening Guthrie Card that is requested for all babies in Australia. This blood could be drawn from a heel prick or from the cut end of the umbilical cord of the placenta in case of a fresh stillbirth (< 7 days between intrauterine death and birth).

Terminal of pregnancy for fetal abnormalities

In cases where a termination of pregnancy has been carried out for fetal malformation, an autopsy may still be desirable to confirm the diagnosis or discover unexpected associated malformations.

Congenital abnormality

Investigations to be performed when an intrauterine fetal death occurs in conjunction with a known fetal abnormality:

- Genetic testing - preferably on amniotic fluid obtained by amniocentesis since this provides the least contaminated sample, but if maternal consent for this cannot be obtained then on cord blood (if obtainable) or fetal skin.
- Maternal serology for syphilis, cytomegalovirus, toxoplasma, herpes and parvovirus. Serum should be taken and forwarded with the baby. Investigation for congenital infection should be pursued if abnormalities indicative of infection are found (for example, hydrocephalus, hepatomegaly, cataracts, fetal hydrops, calcification of brain or placenta).
- Maternal screen for blood group antibodies – forward serum with baby for later investigation if hydrops is evident at autopsy.

Vasculopathies

Pre-eclampsia, placental abruption and intrauterine growth restriction.

All should have a thrombophilia screen comprising –

1. At time of delivery:
   - Anti-cardiolipin antibody
   - Lupus anticoagulant (diagnosis of antiphospholipid antibody syndrome requires at least 2 positive tests of moderate to high titre)
   - Factor V Leiden gene mutation, prothrombin gene mutation

2. At three months post-partum:
   - Homocysteine - may be done earlier if follow-up uncertain.
   - Protein S (a formal diagnosis of protein S deficiency requires 2 abnormal results at least six weeks apart outside of pregnancy)
   - (Note: MTHFR testing, as listed in the ‘Thrombophilia studies 8-12 weeks postpartum’ section of the ‘Stillbirth investigations algorithm’, is no longer routinely performed in South Australia)

Pre-eclampsia

Those with early onset pre-eclampsia (< 28 weeks) should also have

- Anti-nuclear antibody
- Fetal genetic testing (see “Congenital abnormality”)

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**Placental abruption:** In cases of *placental abruption*
> a history of trauma, including domestic or other violence, should be sought.
> Testing for fetomaternal haemorrhage and D-dimers is indicated if the diagnosis is in doubt.

**Intrauterine growth restriction (IUGR):**

Where *intrauterine growth restriction* is evident without further evidence of a vasculopathy, the following should be performed in addition to the thrombophilia screen:
> Maternal serology for cytomegalovirus, toxoplasma and rubella (if not immune) on held maternal serum
> Fetal genetic testing (see “Congenital abnormality”)
> Maternal urinary drug screen as well as a drug-related history

**Intrapartum stillbirths**

> If associated with pre-eclampsia, intrauterine growth restriction and/or abruption follow the placental vasculopathy protocol.
> In the absence of obvious causes, test for fetomaternal haemorrhage and cord (or heart) blood for haemoglobin, platelets and nucleated red blood cells

**Unexplained stillbirths**

In the absence of discernible factors pertaining to fetal demise, or any obvious congenital abnormality, in addition to the “Core investigations” the following should be conducted:
> Cord blood bile acids if possible
> Maternal thyroid stimulating hormone
> Maternal serology for syphilis, cytomegalovirus, toxoplasma, herpes, parvovirus and rubella (if not immune) on held maternal serum
> Microbiology - fetal throat swab, placental intermembranous swab
> Drug history and urine drug screen
> Cord or heart blood - haemoglobin, platelets, nucleated red blood cells, blood group (for anti-D if mother is Rhesus negative).
> Maternal antibody screen
> Fetomaternal haemorrhage testing
> Check mother’s history for the possibility of tropical infectious disorders. Where there is a history of a recent visit to a tropical area, contact infectious disease specialist with regard to required investigations
Abbreviations

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<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
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<tr>
<td>FACS</td>
<td>Fluorescence-Activated Cell Sorting</td>
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<tr>
<td>g</td>
<td>Gram(s)</td>
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<tr>
<td>IUGR</td>
<td>Intrauterine growth restriction</td>
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<tr>
<td>MTHFR</td>
<td>Methylene tetrahydrofolate reductase</td>
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<tr>
<td>PSANZ</td>
<td>Perinatal Society of Australia and New Zealand</td>
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