1. Purpose

Thalassaemias and abnormal haemoglobins are detected in approximately 4% of patients of reproductive age attending the Women's. In almost half of these cases, the abnormality is not evident following simple full blood examination and is only detected by haemoglobin electrophoresis.

These disorders have been described in every ethnic group. They are most frequent in people originating from:

- the Mediterranean basin
- the Middle East
- Africa
- Asia
- Polynesia
- the Subcontinent.

As the inheritance of thalassaemia syndromes is autosomal recessive, the heterozygous carrier states are essentially asymptomatic. Most people are unaware of their carrier state. Depending on the mutation, homozygous or compound heterozygous thalassaemia syndromes may result in adverse maternal outcomes, stillbirth, transfusion dependency, or sickling syndromes.

This document outlines the guideline details for screening couples for thalassaemia to detect those at risk of having children with severe disease, with a view to offering prenatal diagnosis and the option of termination of pregnancy in the event of a positive diagnosis, or to facilitate the early diagnosis and treatment of affected children at the Women’s.

2. Definitions

Haemoglobinopathies- (comprising the thalassaemias and abnormal haemoglobins) are hereditary disorders which affect the balance of globin chain synthesis and/or the structure of haemoglobin.

Thalassaemia- is an inherited condition that affects the production of haemoglobin, which carries oxygen in our blood. It appears in the flowing forms:

<table>
<thead>
<tr>
<th>Thalassaemia Type</th>
<th>Description</th>
<th>Health Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>thalassaemia minor</td>
<td>carrier form - one member of the gene pair is not working properly</td>
<td>no effects on health</td>
</tr>
<tr>
<td>beta thalassaemia major</td>
<td>both members of the beta gene pair are not working</td>
<td>severe anaemia</td>
</tr>
<tr>
<td>alpha thalassaemia major</td>
<td>both members of the alpha gene pairs are not working</td>
<td>Barts Hydrops</td>
</tr>
</tbody>
</table>

3. Responsibilities

Key personnel involved are Obstetric team, Haematologist.

4. Guideline

4.1. Thalassaemia Screening in the Pregnancy Booking Clinic

Couples attending the Women's for antenatal care should be offered screening for haemoglobinopathies at their first visit, according to the algorithm (refer to Appendix 1).

The aim of the Thalassaemia screening program is to identify couples in which both partners have thalassaemia minor and/or a haemoglobinopathy and who are at risk of having a baby with serious disease. This allows timely prenatal diagnosis and/or early diagnosis and treatment of affected children.
Detailed genetic counseling and family studies are important for future pregnancies.

**4.2. Referring women/partners for thalassaemia and abnormal haemoglobin testing and genetic counseling**

Patients may be directly referred by hospital midwives or medical staff. Referrals from outside practitioners and patient self-referrals are also accepted.

The haematology outpatient clinics accept referrals for the following:

- screening of partners and family members
- diagnosis of pregnancies at risk of major thalassaemia/serious haemoglobinopathies
- coordination and genetic counselling for prenatal diagnosis (in conjunction with the Women’s Genetics Clinic)
- management of pregnant women with thalassaemia disease.

Mothers with thalassaemia disease or severe haemoglobinopathy syndromes require MFM consultant supervision in conjunction with haematologist consultation.

**Note:** Consultation regarding thalassaemia and the haemoglobinopathies is coordinated through the Women’s Genetics Clinic ph: (03) 8345 2180.

For urgent queries, contact the haematologist on call via the Women’s switchboard.

Refer to Appendix 1: Algorithm: Thalassaemia screening and referral in pregnancy.

**4.3. Investigations**

Note: Full Blood Examination (FBE) alone is insufficient as a screening test.

Testing for thalassaemia and abnormal haemoglobins requires:

- FBE
- serum ferritin and
- haemoglobin electrophoresis
- if these results are suggestive of alpha thalassaemia:
  - DNA analysis is indicated.

Screening of at risk patients (from high risk ethnic group, past history of anaemia, or family history of haemoglobinopathy) should occur prior to pregnancy.

Prenatal diagnosis cannot be offered to at-risk couples unless DNA analysis has been performed and the exact nature of mutations has been determined.

If the patient is iron deficient, screening should be repeated after iron stores have been replaced, as iron deficiency may result in an abnormal HbA2 in mild forms of beta thalassaemia minor.

**4.4. Treatment/specific considerations**

Pregnant women in whom beta thalassaemia minor is identified should receive high dose folic acid (5mg daily) throughout pregnancy and lactation as there is some evidence that this is beneficial in optimising haemoglobin levels.

Iron supplements should NOT be given in the absence of documented iron deficiency. Many patients with thalassaemia minor have a mild degree of iron overload and iron supplements do not improve haemoglobin or red cell indices unless iron deficiency is present.

**5. Evaluation, monitoring and reporting of compliance to this guideline**
To be developed.

6. References


- Langlois S, Ford JC, Chitayat D. Carrier Screening for Thalassemia and Hemoglobinopathies in Canada. Joint Clinical Practice Guideline, Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists (CCMG), JOGC, October 2008; 218(950959).

7. Legislation related to this guideline

Not applicable

8. Appendices

Appendix 1: Algorithm: Thalassaemia screening and referral in pregnancy
Appendix 2: FBE findings: thalassaemia and abnormal haemoglobins
Appendix 3: Potentially serious haemoglobinopathies: prenatal diagnosis may be offered
Appendix 4: Consumer information
Appendix 1: Algorithm: Thalassaemia screening and referral in pregnancy

The aim of the Thalassaemia screening and referral program at The Women’s is to identify couples at risk of having a baby with thalassaemia major or a significant haemoglobinopathy (e.g. sickle cell disease).

First Antenatal visit

All women:
- FBE
- Ferritin

Plus any woman with:
- past history: anaemia
- family history: thalassaemia or abnormal haemoglobin
- woman or partner from a high risk ethnic background:
  - Mediterranean
  - Middle East
  - Africa (incl. America/Caribbean)
  - any Asian country including India, Sri Lanka, Pakistan, Bangladesh
  - Pacific Islands
  - South America
  - New Zealand Maoris

MCV≤80.0
OR
MCH≤27.0
AND
Ferritin <15

MCV≤80.0
OR
MCH≤27.0
AND
Ferritin >15

Treat iron deficiency in pregnancy

Test partner

THALASSAEMIA SCREEN
(FBE, ferritin, Hb electrophoresis)

Haemoglobinopathy unlikely to be of significance to pregnancy; urgent review not required

Normal

Possible or confirmed haemoglobinopathy of potential significance to pregnancy

No further action

Automatic referral to Haematology Consultant

Note: Partner testing is the responsibility of the obstetric team and should be performed within 2 weeks of receipt of patient results.

Label request forms with: partner’s full name, DOB and state “partner of” and the patient’s name and UR number.

Thalassaemia results of potential significance to pregnancy will generate automatic referral to a consultant Haematologist.

These appointments are coordinated through The Women’s Genetics Clinic ph: (03) 8345 2180.
Appendix 2: FBE findings: thalassaemia and abnormal haemoglobins

<table>
<thead>
<tr>
<th>FBE findings in thalassaemia and abnormal haemoglobins</th>
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</thead>
<tbody>
<tr>
<td>MCV/MCH reduced +/- anaemia</td>
</tr>
<tr>
<td>beta thalassaemia minor</td>
</tr>
<tr>
<td>alpha thalassaemia minor</td>
</tr>
<tr>
<td>deltalpha thalassaemia minor</td>
</tr>
<tr>
<td>Heterozygous Hb Lepore</td>
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Appendix 3: Potentially serious haemoglobinopathies: prenatal diagnosis may be offered

<table>
<thead>
<tr>
<th>Potentially serious haemoglobinopathies for which prenatal diagnosis may be offered</th>
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<tbody>
<tr>
<td>Homozygous beta thalassaemia</td>
</tr>
<tr>
<td>Homozygous Hb Lepore</td>
</tr>
<tr>
<td>Haemoglobin H disease Hydrops (2 gene deletion plus point mutation)</td>
</tr>
<tr>
<td>Hb Lepore/beta thalassaemia</td>
</tr>
<tr>
<td>Hb O Arab/beta thalassaemia</td>
</tr>
<tr>
<td>HbS/HbC</td>
</tr>
</tbody>
</table>

Some couples may request prenatal diagnosis for HbH disease (3 gene deletion alpha thalassaemia).

Appendix 4 Consumer information

Consumer health information about thalassaemia and abnormal haemoglobins can be accessed from the following website: Thalassaemia Society of Victoria. Click on 'Resources' then 'Fact Sheets'.