Guideline

Thalassaemia and Abnormal Haemoglobins in Pregnancy

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:

thalassaemia minor	carrier form - one member of the gene pair is not working properly	no effects on health
beta thalassaemia major	both members of the beta gene pair are not working	severe anaemia
alpha thalassaemia major	both members of the alpha gene pairs are not working	Barts Hydrops

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

- Davies SC, Cronin E, Gill M, Greengross P, Hickman M, Normand C. Screening for sickle cell disease and thalassaemia: a systematic review with supplementary research. Health Technol Assess 2000;4(3).
- 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

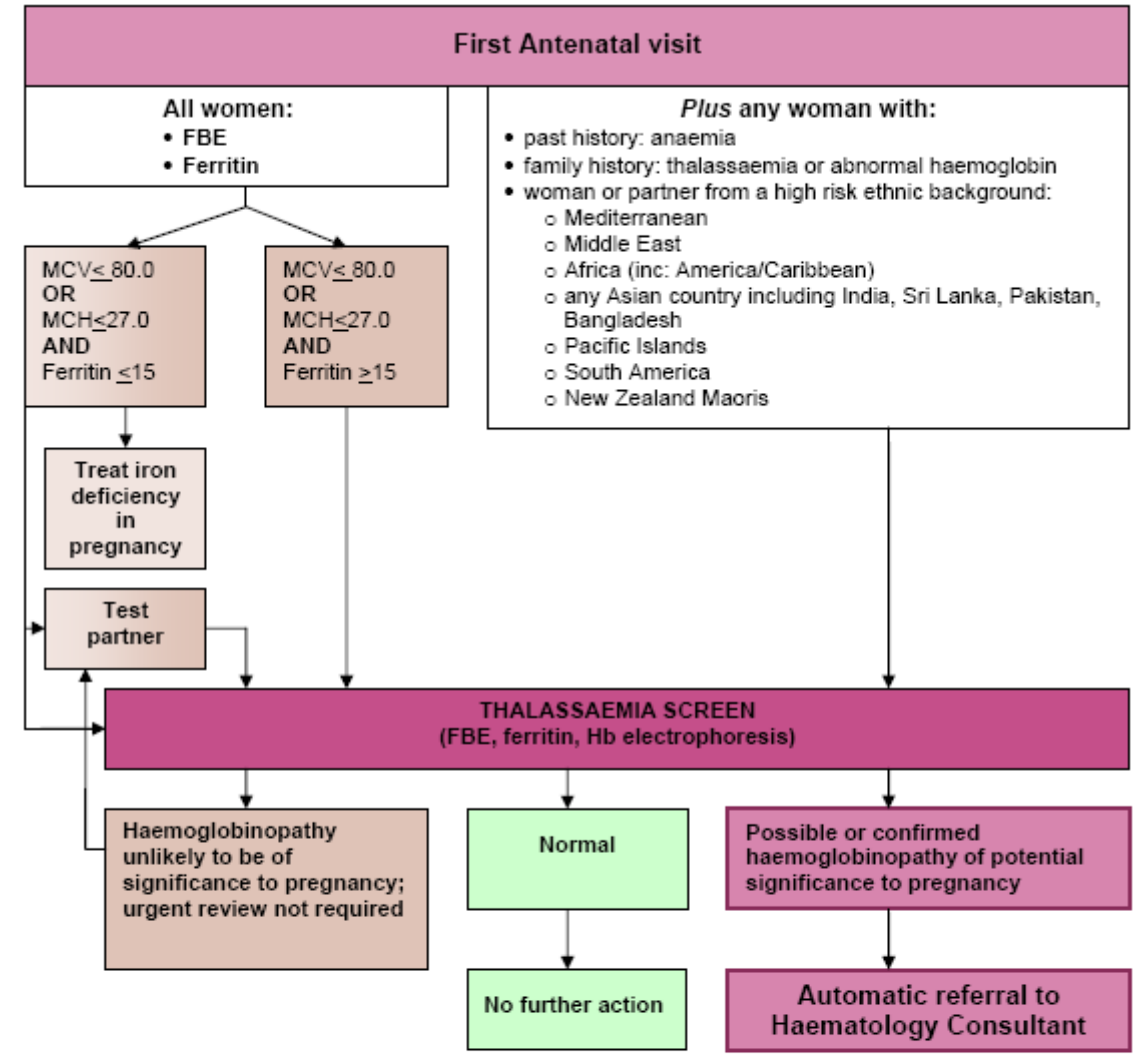
Not applicable

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).



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

FBE findings in thalassaemia and abnormal haemoglobins	
MCV/MCH reduced +/- anaemia	**Often normal red cell indices**
beta thalassaemia minor	Hb S
alpha thalassaemia minor	Hb C
deltabeta thalassaemia minor	HbE
Heterozygous Hb Lepore	Hb O Arab Hb D Hb G Rare variant haemoglobins

Appendix 3: Potentially serious haemoglobinopathies: prenatal diagnosis may be offered

Potentially serious haemoglobinopathies for which prenatal diagnosis may be offered	
Homozygous beta thalassaemia	Homozygous Hbs (sickle cell disease)
Homozygous Hb Lepore	Barts Hydrops (4 gene deletion alpha thalassaemia)
Haemoglobin H disease Hydrops (2 gene deletion plus point mutation)	HbE/beta thalasseamia
Hb Lepore/beta thalassaemia	HbC/beta thalassaemia
Hb O Arab/beta thalassaemia	Hb S/beta thalassaemia
HbS/HbC	HbS/HbD
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'.