7. Fertility and Pregnancy

Principles

- To improve the opportunity for thalassemia patients to have children, if desired.
- To ensure optimal management during pregnancy.

Recommendation

- All children should be closely monitored for pubertal development and endocrinopathies, and appropriately treated by an endocrinologist to reduce the risk of long-term hypogonadism and infertility.
- Patients should be assessed by a fertility clinic and available treatment options discussed.
- Women considering pregnancy should be assessed for risks to mother and fetus, and advisability of pregnancy. Detailed assessment and management prior to pregnancy, and close monitoring of the health of the mother and fetus during and after pregnancy should be ensured.[26-28]
- During pregnancy, women should be managed by a high-risk obstetrician with knowledge of thalassemia-associated risks, and the specialist centre multidisciplinary team including a cardiologist.

Background

As thalassemia care improves overall, patients are living longer into adulthood and are able to attain reproductive capacity. Optimal care of such patients includes addressing infertility and endocrinopathies, optimizing prenatal care, as well as assessing cardiac impairment, liver dysfunction, and the risk of viral transmission. Good overall care during and after pregnancy is vital to improved outcomes for mother and child[441, 442, 455, 456, 457]

Intervention

- All children should be started on a chelation program early in life to reduce iron-associated endocrinopathies especially hypogonadotropic hypogonadism. If identified, endocrinopathies should be appropriately investigated and managed by an endocrinologist.
- When patients reach the age when they may be contemplating pregnancy, a referral to a fertility clinic should be made to discuss options and realistic goals. If the patient is infertile, non-thalassemia causes of infertility should also be sought.
- A couple should be referred to a genetic counselor to discuss the risks of having a child with thalassemia or another hemoglobinopathy. The partner should be tested to determine his/her carrier state for thalassemia and sickle cell disease. The risk of having an affected child and the options for pre-natal diagnosis and subsequent interventions if the fetus is affected should all be discussed with the couple.
- In patients with hypogonadism, ovulation or spermatogenesis may need to be induced and should be done by an experienced fertility centre. Successful pregnancy and fertility are feasible in patients utilising an array of artificial reproductive techniques, more so with females than males[443, 444].

Pre-pregnancy Assessment

- It is possible to undertake HLA typing of IVF embryos to establish a pregnancy that is HLA compatible with an affected sibling with Thalassemia who requires stem cell transplantation[445].
- Fetal genotyping of paternal mutations in maternal plasma from pregnancies at risk of beta-thalassemia can be an option for genetic screening in high risk partners[446].
- There are various blood markers that are altered in HbBarts affected pregnancies, including inhibin-A and PlGF[447,448].

- A thorough pre-pregnancy assessment, prior to considering conception, should include detailed assessment of iron load, cardiac status, liver function, viral infection status, and endocrinopathies[458].
- Several medication changes may need to be made including initiation of folic acid supplements, stopping possible teratogens such as chelation, ACE inhibitors, oral hypoglycemics, and bisphosphonates, and initiating calcium and vitamin D supplementation to prevent worsening of osteoporosis.
- Iron load should be minimized by more intensive chelation before a planned pregnancy due to the fact that transfusion requirements (and iron loading) increase during pregnancy, and iron chelators have to be discontinued at least during early pregnancy. There are a number of case reports of continued oral chelaton in pregnancy, but this is not recommended due to known teratogenic potential of the drug class[449-452].

During Pregnancy

- The patient should be closely followed by the high-risk obstetrician and hematologist through the specialist centre. Cardiac function should be monitored closely and referral to cardiologist needs to take place if patients is at a risk of cardiac complication during pregnancy. Transfusion requirements will likely increase. Serial ultrasounds should be done to monitor for fetal anomalies or growth restriction.
- Significant adverse pregnancy outcomes have been described in HbH disease even when the Hb is maintained >70[452,453].
- MRI to asses iron overload could be performed safely during pregnancy if needed.

Mode of Delivery

- There is a high incidence of delivery by Caesarian-section primarily due to cephalopelvic disproportion[458]. Risks of vaginal and Cesarean-section delivery should be discussed with consideration of other medical issues including cardiac dysfunction.
- Vaginal delivery needs to be encouraged since there is lower risk of cephalopelvic disproportion given adequate transfusion and blood product avaliability

Post-delivery

- The mother should be encouraged to restart chelation with deferoxamine since it is safe while breastfeeding. Calcium and vitamin D should be continued, while bisphosphonates should only be restarted after breastfeeding is stopped. The mother should be advised on the use of contraception or the reinitiation of estrogen replacement therapy after delivery. Post-partum VTE prophylaxis is recommended in NTDT patinets, particularly when splenectomised[454].