Obstetrics – Dr. Rozhan – Lecture 1 - MEDICAL DISEASES WITH PREGNANCY

Most medical conditions in this age group do not result in serious morbidity, though many have the potential to do so, that is, epilepsy, asthma and migraine. It is important that women receive good advice pre-pregnancy about the potential impact of their medical condition and enter pregnancy with appropriate confidence about routine medication or specific management plans to alter treatment in the first trimester

Introduction:
There are a variety of medical disorders which may impact on a mother’s health during pregnancy and the puerperium. These may be classified as those that are incidental to the pregnancy and where no exacerbation is expected as a result of pregnancy and those that are clearly prone to exacerbation due to pregnancy. The latter of greatest concern to obstetricians.

General considerations:
Mean age of childbearing has increased steadily in recent years. This has the effect of increasing the chance of a pregnancy being complicated by coincidental medical conditions and increases the risk that such conditions can impact on women’s health.

Medical diseases complicating pregnancy includes:

1. Haematological abnormalities.
2. Neurological disorders.
3. Respiratory diseases.
4. Heart disease
5. Hypertensive disorders.
6. Renal disease.
7. Gastroenterology.
10. Connective tissue disease.
12. Skin disease.

A. Neurological disorders:
Serious manifestations of neurological disease are fortunately rare in pregnancy, though cerebral haemorrhage remains a significant cause of maternal death. Epilepsy and migraine are common causes of morbidity.

1. Epilepsy:
Approximately 30% of those with epilepsy are women in their childbearing years, which means 1-200 pregnant lady complaining of epilepsy. Pregnancy has no consistent effect on epilepsy: some have increase frequency of fits, others a decrease, and some no difference.

The principles of epilepsy management are that while the risks to pregnancy from seizures out weight those from anticonvulsant medication, seizures should still be controlled with the minimum possible dose of the optimal drug.

Pre-pregnancy counselling: of the patients with epilepsy
1. alter medication according to seizures frequency.
2. reduce to monotherapy where possible.
3. compliance with medication.
4. pre-conceptional folic acid 5 mg.
5. explain risk of congenital malformation.
6. explain risk from recurrent seizures.

Causes of seizures in pregnancy:
1. epilepsy.
2. eclampsia.
3. encephalitis or meningitis.
4. space – occupying lesions (tumour).
5. cerebral vascular accident.
6. metabolic abnormalities (hypoglycaemia).
7. toxic overdose, alcohol withdrawal.
8. cerebral malaria or toxoplasmosis.

Risk of congenital anomaly with epilepsy:
The principle concern related to epilepsy in pregnancy is the increased risk of congenital anomaly caused by anticonvulsant medications, which increase risk two-three fold (5-6%) compared to general population. Approximately doubling of the risk in unexposed epileptic mothers. Epileptic medication are:
1. sodium valproate.
2. carbamazepine.
3. phenytoin.
4. phenobarbitone.

Fetal anomaly includes:
1. neural tube defects.
2. facial clefts.
3. cardiac defect.
4. specific syndrome includes developmental delay, nail hypoplasia, growth restriction and mid-face abnormality.
5. increase chance of epilepsy in offspring of epileptic mothers.

Polytherapy increase the risk (15-25%).

Antepartum managements:
Women of childbearing age who suffer from epilepsy and are on maintenance therapy must have their treatment reviewed and monotherapy is recommended if at all possible.

Antiepileptic drugs can cause teratogenicity and folic acid 5 mg daily throughout the pregnancy is generally prescribed in view of the relative folate deficiency of many mothers on antiepileptic therapy.

It is important that control of seizures is achieved to minimize maternal morbidity (fits can be fatal). Patients must be monitored during pregnancy to ensure that dose adjustments are made as appropriate. Sodium valproate is the major cause for concern in these condition.

All patients should receive anomaly ultrasound assessment to exclude specific abnormalities associated with their medication. These are specifically orofacial clefts, neural tube defects and craniofacial dysmorphism. Vitamin K is recommended to be given from 36 weeks onwards to prevent neonatal bleeding disorders.
Intapartum management:
Epileptic seizures may occur during labour and as such may confuse the diagnostic situation that includes eclampsia. Epileptic seizures should be treated in these circumstances as they would be normally. Vaginal delivery is recommended unless there is obstetric complication.

Postpartum management:
Post-partum drug doses may need to be adjusted if doses have been increased during pregnancy. Specific advice must be given to epileptic women about childcare, for example, not bathing the baby on their own. Breast feeding can be encouraged. Contraception advised: combined oral contraception pill better not used with anti epileptic medication.

2. Migraine:
Headaches are a common problem in pregnancy and migraine sufferers may find their symptoms worsen during the first trimester. Many patients may be using ergot alkaloids to treat migraine prior to the onset of pregnancy and they must be advised not to use these during pregnancy.

Migraines may improve considerably in the second and third trimesters but some patients in who continuing problems exist, the strategies that are employed for prophylaxis are low-dose aspirin, paracetamol and codeine as pain relief and propranolol if attacks continue to be troublesome despite these measures.

B. Endocrine disease
Thyroid disease is the commonest endocrine disorder in pregnant women and this will therefore be considered in more detail than other endocrinopathies. However, pituitary, adrenal and parathyroid disease may have serious consequences for the mother and fetus.

1. Thyroid disease:
Thyroid disease is common in women of child bearing age. However, symptoms of thyroid disease: such as heat intolerance, constipation, fatigue, palpitations and weight gain resemble those of normal pregnancy.

Background
Throid gland: brownish-red, highly vascular gland
Location: ant neck at C5-T1, overlays 2nd – 4th tracheal rings
Avg weight: 25-30 g in adults (slightly more in women)
**enlarges during menstruation and pregnancy**

Physiological changes of thyroid function during pregnancy:
The thyroid hormones thyroxine (T4) and tri-iodothyronine (T3) are synthesized within the thyroid follicles. Thyroid-stimulating hormone (TSH) stimulates synthesis and release of T3 and T4, in addition to uptake of iodide which is essential for thyroid hormone synthesis.

Structure
The gland capsule extend within the gland form septae, dividing it into lobes and lobules
lobules are composed of follicles = structural units of the gland → layer epithelium enclosing a colloid-filled cavity. The colloid contains an iodinated glycoprotein, iodothyroglobulin (precursor of thyroid hormones).

**Physiological changes:**

During normal pregnancy the circulating levels of thyroid binding globulin increase, and as a consequence total T3 and T4 levels also increase. Therefore the free hormone levels should be measured in pregnant women. TSH levels should be interpreted with caution in the first trimester as hCG has a weak stimulatory effect on the TSH receptor.

The fetus cannot synthesize thyroxine until the 10th week of gestation, and it is therefore dependent upon transplacental transfer of maternal hormone. There is increased maternal synthesis of thyroid hormones in the first trimester as a result of transplacental passage and the high levels of thyroid binding globulin.

This in turn results in an increased maternal requirement for iodide. In areas of relative iodide deficiency this may result in the development of maternal hypothyroxinaemia and goitre.

**HYPOTHYROIDISM:**

Hypothyroidism affects approximately 1% of pregnant women. Providing thyroxine replacement therapy is adequate, hypothyroidism is not associated with an adverse pregnancy outcome for the mother or fetus. Poorly controlled hypothyroidism and a variety of adverse outcomes

1. subfertility.
2. congenital abnormalities,
3. hypertension,
4. increased risk of miscarriage
5. premature delivery,
6. fetal growth restriction and
7. post-partum haemorrhage.
8. placental abruption.

Severe hypothyroidism affects the subsequent intelligence of the offspring of affected mothers. Women with hypothyroidism should be given thyroxine replacement at a dose that ensures their thyroid function tests are normal with a FT4 at the upper end of the normal range appropriate for each trimester of pregnancy.

Thyroxine absorption is decreased by certain drugs including iron and calcium supplements. Thyroxine is best taken on an empty stomach and 4 h apart from any iron or other supplements.

**HYPERTHYROIDISM:**

Hyperthyroidism affects 1 in 500 pregnant women, 90% of whom have Graves’ disease. Graves’ disease is caused by TSH receptor stimulating antibodies. Women with well-treated disease rarely have maternal complications of pregnancy.

The disease may remit during the latter trimesters such that treatment may need to be reduced or stopped. In the post-partum period the disease may flare and require treatment with the same or higher doses of antithyroid medication.

Poorly controlled hyperthyroidism is associated with pregnancy complications including:
1. maternal thyrotoxic crisis
2. miscarriage
3. gestational hypertension
4. pre-eclampsia
5. intrauterine growth restriction

The risk of these complications is reduced if the disease is adequately controlled before delivery.

**Treatment of hyperthyroidism:**

The principal drugs used is (propylthiouracil, carbimazole) inhibit thyroid hormone synthesis. A greater proportion of carbimazole enters breast milk, and therefore propylthiouracil is usually the drug of choice if a woman is diagnosed as having hyperthyroidism for the first time during pregnancy.

Both drugs may rarely cause neutropenia and agranulocytosis. Therefore patients should be aware that symptoms of infection, particularly sore throat, may be associated with bone marrow suppression and they must have a neutrophil count checked.

Once drug treatment has been commenced thyroid function tests should be carried out and checked regularly. Propylthiouracil and carbimazole both cross the placenta, fetal hypothyroidism is rarely seen. TSH receptor stimulating antibodies also cross the placenta and may influence the fetal and neonatal thyroid status.

**Thyrotoxic crisis:**

also called ‘thyroid storm’, is a medical emergency that can present with exaggerated features of hyperthyroidism in addition to hyperpyrexia, congestive cardiac failure, dysrhythmias and an altered mental state.

It may be precipitated by infection, abrupt cessation of treatment, surgery, labour or delivery and must be treated immediately as it can be life threatening.

**Treatment of thyrotoxic crisis involves:**

1. administration of intravenous fluids
2. hydrocortisone
3. propranolol
4. oral iodine and carbimazole or propylthiouracil
**MCQ:**

1. Pre-pregnancy counselling of the patients with epilepsy are false except:
   a. stop medication according to seizures frequency.
   b. Increase to polytherapy where possible.
   c. Medication can be stopped if patient has no fit for last two years.
   d. pre-conceptional folic acid 1 mg.

**MCQ**

2. Postpartum management of patients with epilepsy includes:
   a. Post-partum drug doses should be increased.
   b. Breast feeding is contraindicated.
   c. Contraceptive pill better used with anti epileptic medication.
   d. Intra uterine contraceptive device can be used.

**MCQ**

3. poorly controlled hypothyroidism associated with variety of adverse outcomes with pregnancy:
   a. Hypertension.
   b. increased risk of miscarriage
   c. postmature delivery.
   d. ante-partum haemorrhage.
   e. placental praevia.

**MCQ**

4. Regarding hyperthyroidism with pregnancy:
   a. the disease may remit during the first trimesters so treatment may need to be reduced or stopped.
   b. Hyperthyroidism affects 1 in 200 pregnant women
   c. Graves’ disease is the commonest cause.
   d. The principal drugs used is (propylthiouracil carbamazipine) inhibit thyroid hormone synthesis.

**Answers:**

1. C. 
2. d.
3. a,b.
4. c