

A Contemporary Review on Pregnancy Associated Disorders

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Abstract

Pregnancy associated disorders are health problems that are caused by pregnancy. They are very common in pregnancy furthermore; many chronic disorders require special surveillance and intervention in pregnancy. In this we discuss the common pregnancy associated disorders an over view on frequent causes of the pregnancy associated disorders and their management is suggested. Finally a brief review on the risks of various forms of the disorders related to the organ in pregnancy is presented.

Keywords: Pregnancy associated disorders; Heart diseases; Endocrinology; Anaemia

Introduction

There are a variety of medical disorders which may impact on a mother's health during pregnancy and a puerperium [1-5]. Complications of pregnancy are major health problems that may occur during pregnancy. They can also involve the mother's health, along with the baby's health, or both. Some women may have health problems that arise during pregnancy, and other women have health problems before they become pregnant that could lead to complications. It is really very cardinal for women to check health care before and during pregnancy to reduce the risk of pregnancy complications.

Medical disease complicating pregnancy include

- Haematological abnormalities.
- Neurological disorders.
- Respiratory diseases.
- Heart diseases.
- Hypertensive disorders.
- Renal disease.
- Psychiatric disorders.

- Liver disease.
- Connective tissue disease.
- Endocrinology.
- Skindiseases.
- STD.

Haematological abnormalities

Very frequent hematologic complication during pregnancy is anaemia.

A large number of normal physiologic processes occur during pregnancy leads to the term "physiologic anaemia of pregnancy".

Plasma volume mainly increases (40–50%) relative to mass of red cell (20–30%) and mainly accounts for the fall in haemoglobin concentration.

Symptoms

- Feel tired or weak.
- Look pale.
- Feel faint.
- Shortness of breath.

Treatment

Women with pregnancy related anaemia [5-11] are helped by taking iron and folic acid supplements. The increased demand on the bone marrow usually requires women to increase their daily iron intake from 18 mg per day to 27 mg per day.

Neurological disorders

Two-thirds of women usually have no change to the frequency of seizures during pregnancy; one in six will experience improvement, and one in six, deterioration.

Epilepsy is badly associated with maternal deaths (0.5–1 per 100,000 pregnancies) 39 via aspiration or the disorder itself.

Some of them are:

- Eclampsia.
- Metabolic derangement (e.g. hypoglycaemia [12-14], hyponatremia).
- Drug withdrawal.
- Intracranial lesion or mass (e.g. arteriovenous malformation becoming larger with increased blood flow).
- Ischaemic or haemorrhagic stroke.
- Epilepsy.
- Cerebral vein thrombosis.

Safe drugs

- Phenytoin.
- Carbamazepine.
- Phenobarbitone.
- Lamotrigine.

Migraine

Migraine may be associated with the risk of pre-term delivery through co-morbid conditions (e.g. mood disorders) in a subgroup of patients. Importantly, a number of studies have established that migraine is associated with approximately double the risk of developing pregnancy-induced hypertension and preeclampsia, with obesity an additional risk factor [15-21].

Management

- Paracetamol should be tried as a first-line analgesic for headache. Codeine phosphate can be used mainly as an adjunct to paracetamol to increase its analgesic effect. Aspirin (300 mg), acetaminophen, and non-steroidal anti-inflammatories.
- NSAIDs in particular have been linked to fetotoxic effects mainly on the foetal kidneys and premature ductus arteriosus.
- Sumatriptan is a member of a class of more selective serotonin agonists with good efficacy for the treatment of migraine attacks.

Respiratory Disorders

Asthma

Asthma is one of the most common medical conditions in the U.S. and other developed countries. It means to have an exacerbation (attack). You may wheeze, cough, or have difficulty breathing. Remember that the foetus (developing baby) in your uterus (womb) depends on the air you breathe for its oxygen. When you have an asthma attack, the foetus may not get enough oxygen. This can put the foetus in great danger. The risk to the foetus from most asthma medications is tiny compared to the risk from a severe asthma attack.

Dyspnea

Physiologic dyspnea can occur early in pregnancy and does not interfere with daily action.

The main mechanism of dyspnea in pregnancy is controversial. Initially, it lead to breathlessness was attributed to an increased mechanical load by distortion of chest wall from the gravid uterus.

Dyspnea can begin before any upward displacement of the diaphragm, suggesting that main factors other than mechanical pressure may be involved. All other studies support that physiologic dyspnoea is due to a change in perception of normal respiration.

Finally, dyspnea may results from the subjective awareness of hyperventilation that is universally present in pregnancy.

Treatment

- Beta-2 agonist.
- Inhaled corticosteroids.
- Long lasting adrenergic agonist–salmeterol, formoterol.
- Theophylline.

Tuberculosis in pregnancy

In reproductive-aged women there is a significant risk for both tuberculosis infection and disease. With prompt diagnosis and early institution of proper therapy, a good outcome for the mother and child will occur. Many pregnant patients are good candidates for screening for tuberculosis infection, and some should receive preventative therapy before delivery (**Table 1**).

Table 1: Drugs used in pregnancy.

Drugs	Dose (mg/kg)	Side effect
Rifampicin (R), cat C	10	Hepatotoxicity, Nephrotoxicity, Thrombocytopenia
Isoniazid (H)	5	GI Effects, Hepatitis, Peripheral Neuropathy
Pyrazinamide (Z)	20-25	Hepatotoxicity, Nephrotoxicity, Thrombocytopenia
Ethambutol (E)	15	Retrolubar neuritis, Peripheral Neuropathy

Valvular disease

In women of childbearing age valvular disease is often congenitally acquired. Rheumatic heart disease, myxomatous degeneration, previous endocarditis, bicuspid aortic valves are also encountered. Pregnancy complicated by valvular heart disease tends to have a favourable prognosis if risks are appropriately managed

If medical intervention is mandatory during pregnancy, the lowest adequate therapeutic dose of the needed medication should be used.

Medications such as hydralazine, methyldopa, digoxin, adenosine, Procainamide can be used safely in pregnancy.

Above mentioned are contraindicated during pregnancy regardless of the indication.

Angiotensin Converting Enzyme (ACE) inhibitors.

Amiodarone, Angiotensin receptor blockers, and Nitroprusside.

Cardiomyopathy

HCM may be identified by a systolic ejection heart murmur that increases with Valsalva manoeuvre, by increased QRS voltage on the ECG, and/or by abnormal wall thickness and Doppler blood flow by echocardiography.

This disease is widely variable and pregnancy may increase the morbidity and mortality associated with this condition.

Syncope may occur from left ventricular outflow tract obstruction, arrhythmias, or myocardial ischemia or infarction. The incidence of arrhythmias and syncope were not found to be increased during pregnancy.

Management

- Beta blockers.
- Diuretics.
- Calcium channel blockers.

Coronary artery disease

Pregnancy contributes to these risk factors by increasing total cholesterol, low-density lipoprotein, and triglycerides, and decreasing high-density lipoproteins more frequently as a cause for acute myocardial infarction in pregnant than in non-pregnant patients [22-25].

Treatment

- 100 mg aspirin.
- Beta blockers.
- Calcium channel blockers.

Endocrinology

- Pregnancy has a profound impact on the thyroid gland and thyroid function since the thyroid may encounter changes to hormones and size during pregnancy.
- The thyroid diseases hyperthyroidism and hypothyroidism are relatively common in pregnancy and important to treat.
- During pregnancy, if you have pre-existing hyperthyroidism or hypothyroidism, you may require more medical attention to control these conditions during pregnancy, especially in the first trimester.
- Untreated thyroid diseases in pregnancy may lead to premature birth, preeclampsia (a severe increase in blood pressure), miscarriage, and low birth weight among other problems.

Hyperthyroidism

Symptoms of hyperthyroidism may mimic those of normal pregnancy, such as an increased heart rate, sensitivity to hot temperatures, and fatigue.

Other symptoms of hyperthyroidism include the following:

- Irregular heartbeat.
- Nervousness.
- Severe nausea or vomiting.
- Slight tremor.
- Trouble sleeping.
- Weight loss or low weight gain for a typical pregnancy.

Hypothyroidism

Symptoms of hypothyroidism, such as extreme tiredness and weight gain, may be easily confused with normal symptoms of pregnancy.

Other symptoms include:

- Constipation.
- Difficulty concentrating or memory problems.
- Sensitivity to cold temperatures.
- Muscle cramps.

The most common cause of maternal hyperthyroidism during pregnancy is the autoimmune disorder Grave's disease. The most common cause of hypothyroidism is the autoimmune disorder known as Hashimoto's thyroiditis.

Treatment

Hyperthyroidism: They are:

- 1 g Propylthiouracil orally/RT, then 200 mg Q6H.
- 500 mg–1 g Sodium iodide or 8 drops of supersaturated KI.
- Dexamethasone 2 mg iv Q6H for 4 doses. β blockers for tachyarrhythmia's.

Hypothyroidism: They are:

- Treated with 50-100 μ g/day with TFT at 4-6 week intervals.
- Dose adjustment with 25-50 μ g till TSH maintained around 2.5 mIU/L (1st trimester) and 3.0 mIU/L (2nd and 3rd trimesters).

Renal Disorders

Chronic renal disease, although uncommon, can have a major impact on the outcome of pregnancy.

Changes in anatomy during pregnancy:

- Increase in renal size.
- Marked pelvicalyceal system dilatation.
- Renal plasma flow increases early in pregnancy and reaches a maximum by the second trimester.
- Glomerular Filtration Rate (GFR) increases significantly and, therefore, serum levels of creatinine and urea fall.

- Proteinuria is an indicator of renal impairment in pregnancy.

Management

Dose of erythropoietin need to be increased by 50–100% to maintain the haemoglobin between 10–11 g/dl.

Intake of protein can be increased to 1.5 g/kg/day in women on haemodialysis and 1.8 g/kg/day in women on peritoneal dialysis.

Requirement of calcium in these women is around 1.5 g/day.

Pregnancy in women with kidney transplants: Pregnancy in women following renal transplantation has become commonplace. Transplantation restores fertility, and most of women with kidney transplants can deliver successfully.

Recommended kidney transplant recipients immunosuppression includes:

- Prednisone—Less than 15 mg per day (mg/day).
- Azathioprine—2 mg/kg/d or less.
- Calcineurin inhibitor—based therapy at appropriate therapeutic levels.
- Breast-feeding on cyclosporine is not recommended; tacrolimus may be taken during breast-feeding though monitoring of infant levels is recommended.
- Mycophenolate mofetil and sirolimus should be discontinued for 6 weeks prior to conception.

Gestational diabetes

It is mainly caused by increase in blood sugar levels during pregnancy.

In pregnancy women placenta mainly supports the baby as it grows. Hormones from the placenta help the baby develop. But these hormones also block the action of the mother's insulin in her body. This problem is called insulin resistance. Insulin resistance makes it hard for the mother's body to use insulin. She may need up to three times as much insulin.

However, untreated or poorly controlled gestational diabetes can hurt your baby too. When you have gestational diabetes, your pancreas works overtime to produce insulin.

So extra blood glucose goes through the placenta, giving the baby high blood glucose levels. This causes the baby's pancreas to secrete extra insulin.

This can lead to macrosomia, or a "fat" baby. Babies with macrosomia face health problems of their own, including damage to their shoulders during birth.

Management

Blood glucose level targets are between 4-6 mmol/L (fasting).

If healthy eating and physical activity cannot control gestational diabetes, insulin injections will be necessary for the rest of the pregnancy.

STD infections: Sexually Transmitted Infection (STI) sometimes referred to as a sexually Transmitted Disease (STD) is a bacterial or viral illness that you can get from having genital, oral, or anal sex with an infected partner. Sexually transmitted diseases may mainly cause devastating consequences to the baby that includes:

- Mainly stillbirth.
- Reduced birth weight.
- Infection of eye called conjunctivitis.
- Pneumonia.
- Neonatal sepsis.
- Brain damage or motor function disorder.
- Deafness, blindness, or other congenital abnormalities.
- Meningitis.
- Acute hepatitis.
- Cirrhosis.
- Chronic liver disease.

Hypertensive Disorders

The most common medical problem encountered during pregnancy, complicating 2-3% of pregnancies. Hypertensive disorders mainly during pregnancy are classified into 4 categories, as recommended by the National High Blood Pressure (NHBP).

They are:

- Chronic hypertension.
- Preeclampsia-eclampsia.
- Preeclampsia superimposed on chronic hypertension.
- Gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy).

Skin Diseases

Along with the above changes skin is also affected in pregnancy.

Hyperpigmentation

This condition is the darkening of the skin which is caused by increase in the melanin levels. During pregnancy there will be excess production of melanin.

Melasma or chloasma: It is the form of hyperpigmentation which is characterised by tan, brown patches mainly on the face this may be also known as 'mask of pregnancy'.

Treatment: It includes:

- Hydroquinone.
- Sunscreen lotion with SPF at least 30 min when outside.

Pruritic urticarial papules and plaques of pregnancy (PUPPP): It is characterised by pale red bumps on the skin. This lesion can cause itching, burning. In pregnancy these lesions can appear on abdomen, legs, arms, buttocks.

Treatment: It includes:

- Antihistamines.
- Topical corticosteroids.

For relief: Measures to take are:

- Wash with Luke warm water.
- Apply wet clothes or cool compresses.
- Wear light weight clothes.
- No application of soap to the affected area.

Skin tags: It is normally a small flap of tissue that hangs off the skin mainly by connecting stalk. These are usually found on the back, neck, chest, under the breast and almost in the groin regions. They are benign and pain les unless something rubs against them.

Treatment: Skin tags usually removed by electro surgery.

Acne, psoriasis, Atopic dermatitis: All of these conditions can worsen with pregnancy, and also improve after the birth of the baby.

Liver Diseases

As liver serve the multiple functions, hepatic diseases rarely occur during pregnancy.

The commonly occurring hepatic diseases include:

- Preeclampsia.
- HELLP.
- Hepatic Cholestasis.
- Acute fatty liver of pregnancy.
- Hepatitis.

Preeclampsia: It is characterised by high blood pressure usually begins after 20 weeks of pregnancy.

Signs: It includes:

- Excess protein in your urine (proteinuria) or additional signs of kidney problems.
- Severe headaches.
- Upper abdominal pain.
- Decreased urine output.
- Reduced levels of platelets in your blood (thrombocytopenia).
- Impaired liver function.
- Shortness of breath, caused by fluid in your lungs.

Causes of this abnormal development also may include:

- Inadequate blood flow to the uterus.
- Damage of blood vessels.
- A problem mainly with the immune system.
- Certain genes.

Treatment: Involves:

- Anti hypertensives.
- Corticosteroids.
- Anticonvulsants: Magnesium sulphate.
- Bed rest.
- Hospitalization.

In severe cases near the end of pregnancy delivery is recommended.

HELLP: HELLP syndrome is a life-threatening pregnancy complication generally considered being a variant of preeclampsia.

- H (Haemolysis is the breaking down of red blood cells).
- LP (Low platelet count).
- EL (Elevated liver enzymes).

HELLP syndrome symptoms: Physical symptoms of HELLP Syndrome may see at first as Preeclampsia.

- Swelling.
- Headache.
- Vomiting /Nausea/Indigestion with pain after eating.
- Chest or Abdominal tenderness and upper right upper side pain (from liver distention).
- Pain in Shoulder or pain when breathing deeply.
- Bleeding.
- Vision changes.
- High blood pressure.
- Protein in the urine.

Treatment of HELLP syndrome: Most often, the exact treatment for women with HELLP Syndrome is the delivery of their baby. Mainly during pregnancy, many women suffering from HELLP syndrome require a transfusion of some form of blood product (red cells, platelets, plasma). Use of Corticosteroids in early pregnancy to help the baby's lungs mature.

Hepatic cholestasis

Cholestasis is an inability of the liver to excrete bile. It is mainly characterised by itching due to the bile salts deposited in the skin. It is most common in the last trimester of pregnancy when hormones are at their peak but it usually goes away after delivery.

Treatment for pregnancy cholestasis aims to relieve itching and prevent complications.

Prescription medication ursodiol usage (Actigall, Urso), which helps to decrease the level of bile in the mother's bloodstream, relieves itchiness and may also reduce complications for the baby.

Have to soak itchy areas in lukewarm water.

Acute fatty liver in pregnancy

It is the serious condition that occurs in third trimester [1 in 13,000 pregnancies] this can lead to liver failure and encephalopathy. This can progress as jaundice.

Symptoms

- Fatigue.
- Nausea.
- Vomiting.
- Abdominal pain.

Management

Maternal stabilisation should be achieved which includes airway management, treatment of hypertension, hypoglycaemia, electrolyte and coagulation abnormalities. Frequent foetal assessment is important.

After stabilisation delivery of the foetus is preferred.

Liver transplantation is rarely performed for AFLP.

Hepatitis

Pregnant women are also susceptible to viral infection such as hepatitis A-C, and E out of these only hepatitis B and C can lead to chronic disease and could be pre-existing. There are safe and effective vaccine against hepatitis A and B only (Table 2).

Table 2: Drugs used in pregnancy.

Drug	Pregnancy Category
IFN alfa-2b	C
PegIFN alfa-2a	C
Adefovir	C
Entecavir	C
Lamivudine (Epivir)	C
Telbivudine (Tyzeka)	B
Tenofovir (Viread)	B

Nausea and vomiting

Usually it begins in the first 1-2 weeks, reaches a maximum at about 10th week and resolves by 14th week of gestation.

It usually worse in the morning but can occur any time during the day.

The cause of morning sickness is unknown but its occurrence and severity are related to the levels of chronic gonadotropin.

The patient also examined for other causes of nausea and vomiting such as pyelonephritis.

Counselling points

Woman should be advised to eat small, frequent, dry meals, and to avoid fatty foods and other food that create problems.

Treatment

Pyridoxine (50-100 mg)-vitamin B6.

Antihistamines– meclizine, promethazine, prochlorperazine.

Psychogenic vomiting

It can be self-induced or it can occur involuntary response that the person consider threatening or distasteful.

Constipation and diarrhoea

Digestive difficulties, such as constipation and diarrhoea, may occur frequently during pregnancy. Blame it on shifting hormones, changes in diet, and added stress. The fact is, pregnant women deal with diarrhoea quite a lot. Main causes are diet changes, hormonal changes, prenatal vitamins etc.

First choice: Includes:

- Bulk forming agents.
- Laxatives.

Second choice: Includes:

- Milk of magnesia.
- Hyper osmotic agents.

Diarrhoea treatment

Safe drugs in pregnancy: Anti-diarrheal drugs are generally safe to use in pregnancy which are mentioned below:

- Loperamide.
- Antibiotics: Penicillin, cephalosporin's, erythromycin, metronidazole (Flagyl).
- Pedialyte and Gatorade (rehydration solutions).
- Mild diarrhoea usually does not need any treatment since it subsides on its own. BRAT diet (Dry toast, bananas, soft rice, applesauce and) may be given.

Urinary tract infections

Pregnancy causes enormous changes in the body of women. Changes in hormonal and mechanical mean increase the risk of urinary stasis and vesicoureteral reflux. These changes, along with an existed short urethra and difficulty with hygiene due to pregnant belly, also increase the frequency of Urinary Tract Infections (UTIs). Pregnant persons are immunocompromised UTI hosts due to the physiologic changes which are associated with pregnancy. All these changes increase the risk of characterised infectious complications from symptomatic and asymptomatic urinary infections even also in healthy pregnant women.

Treatment

Therapy in first-line: Involves:

- 100 mg Oral Nitrofurantoin monohydrate/macro crystals twice daily for 5-7 days.
- 500 mg oral Amoxicillin twice daily (alternative: three times daily 250 mg orally) for 5-7 days.
- 500/125 mg oral Amoxicillin-clavulanate twice daily exactly for 3-7 days (alternative: three times daily 250/125 mg orally for at least 5-7 days).
- 500 mg oral Cephalexin twice daily for 3-7 days.

Therapy in second-line: Involves:

- Single dose of 3 g Fosfomycin with 3-4 oz of water.

Drugs considered being safe in pregnancy: Involves:

- Some antibiotics namely Amoxicillin, Ampicillin, Cephalosporin, Erythromycin (not isolate).
- Levothyroxine.
- Acetaminophen.
- Like Folic Acid and Vitamin B6.
- Methyldopa, and hydralazine.
- Insulin.
- Heparin.

Drugs that are mainly contraindicated in pregnancy: Some of the drugs in category X that are contraindicated mainly in pregnancy and their effects on the fetus are enlisted below:

- Vitamin A and also its derivatives-Acitrein, Accutane (Isotretinoin), Etreinate—causes Birth defects, miscarriage.
- Thalidomide—Gives as Seal like limbs and other defects.
- Diethylstilbestrol—Mainly Causes cancer vaginal cancer or cervix in female children during their early teenage.
- Warfarin—Causes most multiple birth defects.
- Danazol—Causes female fetus sex organs malformations.
- Oral contraceptives- May cause birth defects.
- Testosterone-Can cause birth defects.
- Methotrexate—Causes multiple defects along with cleft palate.
- Dutasteride-Affects the male fetus sex organ development.

Drug side effects during pregnancy are listed below:

Involves:

- Tetracycline's—Mainly deposited in fetal bones and retards their growth and also affects teeth causing them to be discolored and deformed.
- Chloramphenicol causes Gray baby syndrome.
- Isoniazid-Neuropathy and seizures mainly in fetus, mother's liver damage.
- Sodium Valproate—nervous system defects.
- ACE inhibitors—birth defects, growth retardation, fetal death.
- Lithium—Mainly effects fetal thyroid.
- Androgens—Causes Multiple defects.

Conclusion

According our findings pregnancy associated disorders like etc. to be effected during pregnancy so that regular care should be taken during pregnancy according to the physician advice regarding the medications and diet etc. The main drugs avoid during pregnancy are acne medications, tranquilizers, MAO inhibitors.

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