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# Medical Diseases During Pregnancy

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**Abbreviations:** CGM: Continous Glucose Monitoring; PCOD: Polycycstic Ovary Disease; HAPO: Hyperglycemia And Adverse Pregnancy Outcome; ACE: Angiotensin Converting Enzyme; ARB: Angiotensin Receptor Blocker; TPO: Thyroid Peroxidase

## Mini Review

Health care and management have evolved over time. We have developed health care protocols for most of the disorders. But pregnancy, child birth and lactation remains an area that do not have fixed protocols. However general guidelines are there and we need to indiviualize the care. Further in pregnancy, the treatment need to be tailored and continous adjustments need to be made based on the evolving preganacy, changing hormone status, fluid retention, weight gain and the sudden exodus of products of conception and sudden reversal of all the processses. We need to be more careful in such patients also because it involves mother as well as the foetus and newborn. This review will take you through the diseases and disorders , commonly faced by physicians while treating a pregnant patient and guide the clinician in making important clinical decisions.

As we alll know that obesity in evoloving epidemic in most of the developed world as well as in middle east. A lot of obese diabetic patients are coming with pregnancy. Diabetes care must be planned in advance.Insulin remain the drug of choice during pregnancy. Patients blood sugars must be controlled atleast 3 months before conception. An HbA1c of 7 % is acceptable before pregnancy but effort should be made to lower it to 6.5% [1]. However during pregnancy, effort should be made to keep it below 6.%, If it can achieved without hypoglycemia. Insulin requirement increases exponentially in 2$^{nd}$ and 3$^{rd}$ trimester , so you might need to see patients more frequently. Self monitoring is encouraged and target blood sugars must be < 95mg fasting, <140mg after 1 hour and <120mg after 2 hours. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) trial has shown that increasing levels of glycemia have been associated with adverse outcome in pregnancy [2]. Regular Insulin , NPH insulin, Insulin Lispro, Insulin Aspart and Insulin determir are all acceptable to be used in Pregnancy. Insulin Glargine, Insulin Degludec have not been thorougly tested in pregnancy [3]. In patients with Type 1 Diabetes, continous glucose monitoring (CGM) and better control has been associated with better outcomes. However CGM may not be avaialble everywhere and it does not replace the standard care, regular follow up and self monitoring of blood sugars. . Patients with diabetes, both Type 1 and type 2 are associated with higher risk of pre-eclamsia, so all such patients must be given, Aspirin 75 to 150mg (mostly 81 mg) after 12$^{th}$ week of Pregnancy (Grade 1 recommendation). Insulin requirement falls to almost 50% of pregnancy level immediately after delivery and may return to prepregnacy level within 2 weeks. So this period need a continous monitoring and reassessment to avoid hypoglycemia by excessive insulin dose. Many of our patients have Polycycstic Ovary disease (PCOD) and are on Metformin to induce ovulation. All such patients must be taken off Metformin by the end of First trimester.

Another common condition,seen in pregancy is Hypertension. Certain drugs have been known to cause serious issues in pregnancy. Angiotensin Converting Enzyme (ACE) inhabitors and Angiotensin Receptor Blocker (ARBs) can cause foetal renal dysplasia, oligohydoamnios, pulmonary hypoplasia and intrauterine growth retardation, so these drugs are not recommended in pregnancy. Statins also must be stopped at conception. Chronic diuretic therapy may cause placental insufficiency due to hypoperfusion. Drugs safe in pregnancy are Methyldopa, Nifedepine, Diltiazem,

Labetolol and Clonidine. A target blood presure must be less than 135 /85mmHg, but above 120/80mmHg. Both higher and lower levels can be detrimental. All hypertensive patients who have a risk of developing preclamsia must be started on Aspirin, 75 to150mg (mostly 81mg) anytime after 12 weeks and stopped at the end of pregnancy [4].

A clinical spectrum of *preclampsia*, eclampsia and HELLP syndrome is another challenging morbidity associated with pregnancy. *Preclampsia* is defined as a new onset gestational Hypertension (usualy in 2nd trimester) of more than 130/90mmHg, on two separate occasions, after an interval of 4 hours, when it is associated with a proteinuria of 300mg /24 hours or more. Many such patients have peripheral edema as well. However sometimes proteinuria is missed or does not appear, the following signs and symptoms might be present. Platlet count of <100,000, Creatinine level of more than 1.1 mg or doubling of creatinine from baseline, Urinary Protein /creatinine ration of >0.3, 1+ protein on dipstick, liver enzynes more than twice the upper limit of normal, or an unexplained nonresolving right hypochondrial or epigastric pain (without clear reason), new onset visual or cerebral disturbances or pulmonary edema. All such patients can be labelled as having preclamsia. If blood presuure is >160/110, it is called *severe preclampsia* and if the patients throws a convusion, it is called *Eclampsia.* When a Hemolytic Anemia is associated with Preclamsia, it is called *HELLP syndrome* (Hemolytic Anemia, Elevated Liver Enzymes and Low Platlet Count). Danger to the life of both foetus as well as mother increases progressively with progression of disease process. Early *preclampsia* can be treated conservatively up to 37 weeks of gestation but severe eclampsia is delivered by 34 weeks. Eclampsia is an emeregency and decision has to be take quickly to keep the life of both mother and foetus in mind. Complete bed rest, control of blood pressure by approved drugs, and planning of early delivery of foetus can save the life of both mother and the baby. Steroids are given to accelrate the lung maturity in the foetus, to avoid hyaline membrane disease of newborn, but blood pressure or even blood sugars may shoot up by steroid , so a close monitoring and management of these parameters is to be done meticulously. Seizures are usually treated by Magnesuim Sulphate 4 grams over 10 minutes by infusion pump, followed by 1 gram per hour for 24 hours after last seizure. Recurrent seizure may necessitiate increasing the maintainance dose of Magnesium sulphate to 1.5 to 2 grams per hour. This is to be continued for 24 hours after delivery. Blood pressure comes down progressively but may take upto 12 weeks to return back to baseline. All such patients need to be assesed for improvement of Platlet count, Liver function, kidney functuion before thay are discharged from hospital [5].

Other commonly encountered disorder during pregnancy is Hypothyroidism. Cut off levels for Thyroid Stimulating Hormone (TSH) are lower in pregnant females than in nonpregnant ones. Autoimmune hypothyroidism with anti-Thyroid peroxidase (TPO) antibodies have higher adverse pregnancy outcomes. TSH must be kept below 2.5uU/L, in all such cases. Frequent monitoring is required and thyroxine requirement increases by 25 to 50ug till the end of 3rd trimester. Following delivery patients can be managed with baseline requirement (prepregnancy dose) of Thyroxine. Women in Iodine deficient areas who do not have access to Iodized salt or iodised oil must receive 250ug of Iodine daily starting 3 months before conception to avoid adverse pregnancy outcomes and Neurological complications and cretenism [6].

Bronchial Asthma, and community acquired pneumonia are frequently encountered during pregnancy and must be treated by standard protocols. Most of the pencilli derivatives and cephalosporins are safe in pregnancy. Mild Urinary tract infections can be treated safely by amoxacillin and Ceftrioxe is safest parenteral antibiotic for Community Acquired Pneumonia. Ciprofloxacins should be avoided especially during first trimesters because of its cartilage toxicity. Iron deficiency is another common disorder and are treated by oral iron in first trimester, Intravenous iron in second trimester and blood transfusion in 3rd trimester. Hemoglobin levels must be kept as normal as possible and atleast above 10gms % in 3rd trimester. Sickle cell anemia and sickle cell crisis does occur in pregnancy and is treated accorduing to standard protocols. Hydoxy urea is contraindicated during pregnancy and patient must use contraception for atleast 6 months after stopping hydroxy urea, before planning a pregnancy. Malaria in pregnancy is very unique situation. Umcomplicated Falciparum malaria is treated with Quinine and clindamycin. But severe Falciparum Malaria must be treated by Parenteral Artesunate [7]. Vivax Malaria can be treated by Chloroquine but Primaquine is contraindicated in pregnancy. World Health Organization recommendfs Intermittent Prophylactc Treatment (IPTp) by Suladoxine/pyremthamine Combination or by by artesesin based combinations in all pregnancies in malaria endemic areas [8].

Thromboembolic disease is another interesting but life threatening disease that can occur during pregnancy or in post partum period. Patient who have a provoked thrombotic phenemenon before pregnancy can wait for pregnancy till they complete the course of anticoaugulants. Direct acting oral anticougulants (DOAC) have not yet been approved during pregnancy. Warfarin is also contraindicated in first trimester of pregnancy and in last trimester. Warfarin embryopathy is a well known phenemonn, so is the foetal bleeding in third trimester. Unfractionated Heparin (UH) and Low Molecular weight Heparin (LMWH) remains the cornor stone of anticoaugulation during pregnancy for any thrombotic disease. Clexane 1 mg per kg twice a day or Daltaprin 100 units per kg twice a day is the standard dose. UH can also be used twice a day and titrated to keep APTT 1.5 to 2.5 times the baseline APTT and it may need to be increased with increase in weight during last trimester. UH is used only if Creatinine clearance in less than 30 ml/min or patient is waiting for labour and might need a rapid reversal of anticoagulation for surgery. In addition, patients with Antiphospholipid antibody syndrome need additionally, Aspirin 150 mg daily during entire


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pregnancy. Aspirin can be stopped after pregnancy. Sometimes Venous thrombosis occurs for the first time in postpartum period (Phlegma Alba Dolens). This is an emergency and can be limb threatening and life threatenings. It progresses rapidly to cause limb ischemia or even gangrene. It should be treated again with UH infusion or LMWH and may be combined with Thrombolysis, thrombectomy or other surgical methods depending on severity of the thrombosis [9]. Patients with metallic prosthetic heart valves and those who develop Heparin Induced Thrombocytopenia (HIT) must be referred to a haematologist for anticoagulation advice [10,11].

There are many rheumatological disorders that pregnanat patients may come up with. Patients with Systemic Lupus and Rheumatoid artritis patients may need steroids and so may be needed in some resistant Bronchial Asthma patients. There are lot of observational studies on such patients. There is conflicting data regarding the cleft lip with or without cleft palate in patients taking steroids. However there is no data to support that steroids cause any premature delivery, or low birth weight or gestational Diabetes or Gestational hypertension. So pregnant patients must be treated as any nonpregnant patient when it comes to steroids. However the dose and duration of steroids must be kept to minimum required to control the underlying disease. Randomised controlled trials have been seen as unethical on such subject [12].

One of the most challenging disease is seizure disorders. Women with seizure disorders have genuine apprehension of drugs causing major congenital malformation (MCM) and possible risk of seizure, should they stop the drug. Propective registries both in USA and UKA have tried to estimate the frequency of MCM. Highest MCM is seen with Valproic Acid (9.3%, followed by Phenobarbitol (5.5%) Topiramate (4.2%) and Clonazepine (3.0%). These drugs should ideally be avoided in pregnancy. Least MCMs are seen with Levitiracetam (2.4%), Lamotrigine (2.0) and Oxcarbazine (2.2%). These drugs are usually water soluble and have short duration of action. Further the clearance of these drugs increase during pregnancy so levels may fall drastically to ½ to 1/3$^{rd}$ level with advancing pregnancy. So women with seizures may need to be monitored clinically and if possible drug levels must also be monitored more frequently, where possible. None the less ,If patients cannot be controlled by other drugs, valproate can be used but the dose must be kept to less than 700mg per day [13].

There are many more medical conditions that pregnant patients may suffer from and the management of above mentioned disorders may get complicated further. Discussions on thoses aspects will be beyond the scope of this short, concise review. Clinicians must go to relevant resources for more details on these subjects.

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