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A REVIEW ON PREGNANCY AND ITS COMPLICATIONS

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ABSTRACT

It is difficult to prescribe the right medication to pregnant women. Pregnancy of prenatal age is the period in which many complications arises. These complications may include anemia, UTI, loss of pregnancy, eclampsia, gestational hypertension, gestational diabetes, thyroid dysfunction. The women are prescribed with drugs according to food and drug administration (FDA) pregnancy drug list. They categorized drugs as A, B, C, D and X. some drugs are not categorized by FDA, they comes under N (Not classified) category. If these complications are left untreated fetus may develop birth defects or teratogenic effect or congenital mall formations.

INTRODUCTION

Prenatal or antenatal is the developmental process which starts with embryo-genesis which is the fertilization stage and continues with foetus development. Prenatal development is divided or measured in trimesters. They are First trimester, Second trimester, Third trimester. The **first trimester** is the first development stage where the rudiments of all the major organ systems appear. The first trimester lasts from the first day of last period and until the last day of week 12. The changes that occur in the body during first trimester are slight bleeding which is the sign of implantation of embryo in the uterus, breast tenderness is due to hormonal changes, constipation due to slow muscle contractions which is the result of increased levels of progesterone. The **second trimester** is the second developmental stage where almost all the organ systems are completely developed. The second trimester lasts from 14th week to the end of 28th week. By the end the fetus appears with complete human features. The third trimester is the last developmental stage where there is rapid or quick growth of fetus. **Third trimester** lasts from 29th week to the end of 40th week. In the early stages of third trimester most of the organ systems are fully functional.[1]The child bearing age of women is from 15 to 44 years. Periconception care is very much needed to avoid exposure to harmful substances that cause teratogenic effects.[2] Some of the medicines that cause teratogenic effects includes: Isotretinoin (High risk) and ACE inhibitors, barbiturates, narcotic analgesics (Low risk). Thus, it is very important that the prescriber should be well aware of all the drug induced teratogenic effects before prescribing the medicines.[3] The pregnant women are excluded from the clinical trial

studies due to ethical reasons. Due to limited knowledge of drug use in pregnant women there may be higher risk to mother and the fetus as there are limited studies in pregnant women.[4] That is why, for the safe prescribing of drugs in pregnancy USA - Food and Drug Administration has classified drugs into different categories. They are A, B, C, D and X drugs.

Therapeutic approach in pregnant women is not safe and effects drugs risk benefit ratio. The variables that affect the drugs risk benefit ratio are -Fetal age, Dose of drug, Duration of exposure, Drug distribution, Drug metabolism, Drug excretion. Therefore, the prescription should not only base on the category of drug but also on the right drug, right dose, right route of administration, right frequency. As nutritional deficiencies are common in pregnant women, they are commonly prescribed with folic acid supplements, calcium, multivitamin, iron, herbal supplements. Complications in child bearing women are higher and deaths are noted in highly developing countries.[6,7] The most commonly occurred complications in prenatal women are: Anaemia, UTI, Thyroid dysfunction, Hypertension, Diabetes, Eclampsia, Loss of pregnancy and Other conditions like GERD, constipation, diarrhea, nausea, vomiting, itching, PV discharge and bleeding, headache, fever, pains.

ANAEMIA

Present 20% of women develop iron deficiency anaemia or folic acid deficiency anaemia or both. Anaemia occur due to transfer of iron and folic acid to the fetus. According to WHO prevalence of anaemia is 14% in developed countries and 51% in developing countries. Prevalence of anaemia in India is 65-75%. The risk factors for iron deficiency anaemia in pregnancy include per-term delivery, low birth weight, inferior neonatal health. For the expansion of maternal red blood cells, serum ferritin levels fall markedly between 12 and 25 weeks of gestation for the iron utilization. There in two types of anaemia in prenatal period. They are pathological anaemia includes deficiency and haemorrhagic anaemia.

A. Deficiency anaemia includes:

- Iron deficiency anaemia
- Folic acid deficiency anaemia
- Vitamin B12 deficiency anaemia
- Protein deficiency anaemia

B. **Haemorrhagic anaemia includes:**

- Acute haemorrhagic anaemia: Bleeding during early months of pregnancy
- Chronic haemorrhagic anaemia: occurs due to conditions like hookworm infestations, GI bleeding, etc.

Physiological anaemia

Physiological anaemia of pregnancy is caused when disproportionate increase in RBC volume, plasma volume and haemoglobin mass occurs. Haemodilution occurs when plasma volume increases more than RBC mass which leads to physiological anaemia in pregnancy. Criteria for physiological anaemia are:

- RBC 3.2.million/cumm
- Hb- 10 gm%
- Normocytic-normochromic anaemia
- PCV 30%

Signs of anaemia during pregnancy are: there are no signs for mild condition but signs for severe condition includes pallor, glossitis, stomatitis, oedema due to hyperprotenemia. Symptoms of anaemia during pregnancy are weakness, indigestion, loss of appetite, palpitation,

dyspnoea, giddiness and even congestive cardiac failure are seen.

Prevention of iron deficiency anaemia:

- Prophylaxis of non-pregnant women: prevention should start before pregnancy as most of women start their pregnancy with anaemia or low iron stores. 60mg of daily iron dose should be received for 2-4 months, concomitant use of folate will prevent neural tube defects in the new borns.
- Iron supplementation during pregnancy
- Treatment for hookworm infestations
- Improvement of dietary habits
- Improving of bio availability of food iron

According to government of India ministry of health recommends the management for anaemia in pregnancy includes 100mg of elemental iron with 0.5mg of folic acid. [8,9]

URINARY TRACT INFECTION

Urinary tract infection is a very common complication during pregnancy. It is due to growth of microorganisms in urinary tract. Both gram negative and gram positive organisms causes UTI. Examples of gram negative organisms are E.coli, klebsiella, proteus and gram positive organisms are the streptococcus, staphylococcus, enterococcus species. In pregnancy the UIT is of 2 types

- Asymptomatic UTI: Asymptomatic usually involves lower urinary tract.
- Symptomatic UTI: symptomatic usually involves upper urinary tract.

Prevalence of asymptomatic UTI during pregnancy in India accounts for 6.2% and symptomatic UTI accounts for 1-18%.UTI is most common during third trimester also sometimes seen in first trimester. UTI occurs due to short urethra as organism can easily effects the tract, past history of UTI, hygiene, age, etc. Signs and symptoms of UTI are burning micturition, increased urge of urination, increased frequency of urination, abdomen pain and pain while urinating. The organisms from urethra move or travel to the upper urinary tract i.e kidney, if the infection spreads to kidney it shows symptoms like fever, vomiting's, back pain, chills. Antibiotics are prescribed in the treatment of pregnant women they are nitrofurantoin and amoxicillin-clavulanic acid which are B category drugs. [10]

ECLAMPSIA

It is generalized tonic-clonic convulsion that occur during pregnancy. It is one of the major complication during pregnancy but less common in developed countries. The incidence of eclampsia in UK is 4.9 per 10,000 and in USA 4.3 per 10,000. It is higher in India and is 220 per 10,000. Eclampsia occurs mostly during the Third trimester or during labor or Within 10 days of post-partum period. The clinical features of eclampsia are seizures, oedema, vision disturbances, headache. Eclampsia also increases the risk of further complications like abruptio placentae, pulmonary oedema, acute renal failure, pneumonia, cardiac arrest. The management or cure for eclampsia is the usage of anticonvulsants like phenytoin which belongs to category D. [11]

THYROID DYSFUNCTION

Thyroid hormones are important and essential for the fetal growth and development. Their requirement increases during pregnancy. Moderate iodine deficiency is observed in 50% of prenatal women. 25.5% higher than normal daily supplementation is needed to avoid hypothyroidism and goitre. Intrauterine fetal death, thyrotoxic crisis, spontaneous abortion, intrauterine growth reduction, pre-eclampsia is the multiple risk for

embryonal development if hypothyroidism is untreated.

Hyperthyroidism

Grave's disease is common cause of hyperthyroidism and in 2nd and 3rd trimester the manifestation can be expectedly increased. Subacute thyroiditis, toxic adenoma, toxic nodular goitre, carcinoma and drugs like amiodarone lithium are the rare causes of hyperthyroidism. Propylthiouracil PTU (50-100mg/day) of D category is the first choice of drug as it is hepatotoxic liver enzymes should be regularly monitored. Thiamazole (5-20mg/day) of D category which is second choice of drug and should be avoided in first trimester as it is embryotoxic. Beta blockers like propranolol of C category (20-40mg every 4-8 hours) can be given to inhibit conversion of T3 and T4.

Hypothyroidism

Hershimota's thyroiditis and other causes like atrophic thyroiditis, thyrostatic agents, congenital thyroidaplasia, iatrogenic hypothyroidism and rarely hypopitutarism are the causes of hypothyroidism. L-thyroxine at the dose of 1.2-20µgms/kg of body weight is prescribed during pregnancy and lactation period.[12]

GESTATIONAL HYPERTENSION

6-8% of women are affected with gestational hypertension. Hypertension in pregnancy is of 3 types. They are -

- Chronic hypertension
- Gestational hypertension
- Pre-eclampsia

Chronic hypertension: hypertension that occurs before 20 weeks of pregnancy or 12 weeks beyond postpartum. Decreasing of blood pressure leads to reduced placental perfusion. If the blood pressure is greater than 150 to 180/100 to 110mmhg, treatment is necessary to prevent organ damage. Most commonly prescribed medication in the pregnant women for lowering blood pressure are methyldopa (Category-B), Labetalol (C), Nefedipine (C) are given orally.

Gestational hypertension

Gestational hypertension is the increased blood pressure during pregnancy and has replaced the term pregnancy induced hypertension. The women with gestational hypertension are also diagnosed with pre-eclampsia and chronic hypertension. Half percentage of women acquiring gestational hypertension is between 24 to 35 weeks of gestation.

Pre-eclampsia

It is associated with hypertension and protinuria occurs after 20th week of prenatal period. Pre-eclampsia may occur due to abnormal placental implantation, angiogenic factors, cardiovascular maladaptation and vasoconstriction, genetic predisposition, vascular endothelial damage, dysfunction. Pre-eclampsia are prevented by calcium, vitamin, magnesium supplements and omega 3 fatty acids. Aspirin of dose 75-81 mg/day is prescribed to prevent pre-eclampsia for the women with increased risk. Magnesium sulphate also helps in the prevention of pre-eclampsia and also reduces the occurrence or incidence of placental abruption. For the management of pre-eclampsia intravenous Labetalol (C) and Hydralazine (C) are prescribed.[13]

LOSS OF PREGNANCY

Miscarriage is the serious health problem. Miscarriage is the loss of pregnancy that occurs before 20 weeks of gestation. According to reports one out of five women with pregnancy is experienced with miscarriage or loss of pregnancy. Increased risk occurs with maternal age <18 years or >/=35 years due to aneuploidy (presence of abnormal chromosomes in cell).

CATEGORY	DESCRIPTION
A	Controlled studies in humans show no risk to the fetus
B	No controlled studies have been conducted in humans; Animal studies show no risk to the fetus
C	No controlled studies have been conducted in animals or humans
D	Evidence of human risk to the fetus exists; however, benefits may outweigh risks in certain situations
X	Controlled studies in both animals and humans demonstrate fetal abnormalities; the risk in pregnant women outweighs any possible benefit

Table No.1: FDA drug risk classification[5]

Disease	TSH	Free T4	Free T3
Hypothyroidism	High	Low	Low or normal
Hyperthyroidism	Not predictable	Very high	High

Table No. 2: Range of thyroid hormones in pregnant women

Disease	Manifestation
Hypothyroidism	Fatigue, weight gain, cold intolerance, constipation
Hyperthyroidism	Tachycardia, weight loss , heart intolerance, nervousness, tremor, visual disturbance

Table No.3: Clinical manifestation in thyroid dysfunction

Risk of loss of pregnancy includes: increased age, history of loss of pregnancy or infertility. 15% of total pregnancy women experiences spontaneous pregnancy loss.[14,15,16]

GESTATIONAL DIABETES

Gestational diabetes mellitus is the occurrence of diabetes during pregnancy. There is elevated levels of blood glucose levels during prenatal period and is returned to normal level after the delivery. Placenta blocks insulin production from the pancreas and increases the glucose levels in blood leading to hyperglycaemia. The women who are at high risk of acquiring gestational diabetes mellitus are:

- Age greater than 25 years
- Overweight
- Past history of gestational diabetes mellitus
- Large baby (macrosomia)

Gestational diabetes is controlled by tracking glucose levels, diet, exercise or oral hypoglycaemics or by insulin. The offspring of gestational diabetes mellitus women may have problems with breathing, low glucose levels, jaundice.[17]

CONCLUSION

During pregnancy many complications arises, that complications either due to due to pregnancy or consumption of drugs and as there are limited clinical trials in pregnant women it is difficult to prescribe the right medication. This is because the medicine may cause teratogenic effect to the fetus. For the safe pregnancy the physician must have knowledge on drugs use, complications, category of drug use in prenatal period. Clinical Pharmacist can helpful to overcome those problems by their clinical knowledge. Therefore, drugs must be prescribed according to FDA drug risk classification.

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