**ABSTRACT**

Pregnancy is beginning of new life. It start with conception and continues through the fetus and finally ends at birth. It is not illness. Pregnancy is process which results into continuation of the species. Drugs play important role in important role in improving the health and promoting well-being. However to produce desire effect, they have to be safe, efficacious and have to be used. Certain drug given during pregnancy may harmful to unborn child is one of the classical problem in the medical treatment. The main purpose of this review is to prepare a list of safe medications which can be taken during pregnancy with unsafe and highly contraindicated drugs. And also a quick reference for health care professionals. For many drugs, good pharmacokinetic and pharmacodynamic data in pregnancy and parturition are lacking. For other drugs, recent studies demonstrate major pharmacokinetic or pharmacodynamic changes that require dose adjustment in pregnancy, but current dosing guidelines do not reflect these data.

**KEYWORDS:** Drug used in pregnancy, Pharmacokinetic, Drug Categories.

**INTRODUCTION**

Pregnancy is the beginning of new life. It starts with conception and continues through the fetus and finally ends at birth. It is not an illness. Pregnancy is a process, which results into the continuation of the species. Furthermore, pregnancy has a positive influence on the female organism, both physically and psychologically. During gestation, the woman reaches her full physical and mental potential. The use of medications in pregnancy that are not designed nor approved for pregnancy, labor and lactation is called "off-label" use. Pregnancy, whether planned or a pleasant surprise, brings with it important concerns about prescription and over the counter (OTC) drugs. Not every medication poses a risk to unborn baby.
However, some do. The development of knowledge in understanding the use of drugs during pregnancy has been in stalemate in comparison to other areas of therapeutics, mainly due to difficulties in testing new products in pregnant women and paucity of good quality research. These drugs are used only when they are really essential for the mother’s treatment and when no safer alternative is available. Most drugs taken by the pregnant women can cross the placenta and expose the developing embryo and fetus to their pharmacologic and teratogenic effects. Critical factors affecting placental drug transfer and drug effects on the fetus include:

1. The physiochemical properties of the drug.
2. The rate at which the drug crosses the placenta and the amount of drug reaching the fetus.
3. The duration of exposure to the drug.
4. Distribution characteristic in different fetal tissue.
5. The stage of placental and fetal development at the time of exposure to the drug.
6. The effect of drugs in combination.[1]

**Pharmacokinetic changes in pregency**

The drug effect can be changed by the changes pharmacokinetic in pregnancy, hydrophilic drugs are more diluted and distributed In non pregnant women than pregnant women, Increased dose may require, Hydrophobic are more soluble in pregnant women, The free drug have therapeutic or adverse effects on the mother and for placental transfer to the fetus, excretion of drugs increase by kidneys, mainly which are excreted primarily unchanged in the urine (digoxin, lithium), In the pregnancy, the increased size of uterus decreased renal blood flow in supine position, This results in decreased excretion and prolonged effects of renally excreted drugs.

Pregnancy results in extensive anatomical and physiologic changes. Physiologic changes affecting the cardiovascular, respiratory, renal, gastrointestinal, and hematologic systems can significantly alter the pharmacokinetic and/or pharmaco-dynamic profile of drugs used in pregnancy. Specifically, physiologic changes during pregnancy can alter the bio-availability, distribution, and clearance of many drugs.[2]

**Physiologic changes in pregnancy**

Pregnancy occurs when a sperm penetrates an egg. This is called fertilization and usually takes place in the woman’s fallopian tube. The fertilized egg immediately begins to divide into a growing cluster of cells. Between 5-7 days after ovulation the fertilized egg implants into the wall of uterus and starts forming the placenta. The placenta maintains and nourishes
the baby by enabling the transfer of O2, CO2, amino acids, fats, vitamins and minerals from the mother’s blood. It also allows transfer of waste substances from the growing baby. From the time of implantation wall of uterus until approximately eighth week of life the baby is known as embryo. Development is rapid during this stage as the specialized cells begin to form the vital organs, nervous system, bones, muscles and blood. After the eighth week of pregnancy the developing baby is called a fetus.

2.4 cm long with most of internal organs formed and external features such as eyes, nose, mouth and ears start to appear. As the fetus and placenta grow and place increasing demand on the mother, phenomenal alterations in metabolism occur. The most obvious physical changes are weight gain and altered body shape. Weight gain is due to increase breast tissue, blood and water volume in the form of extra vascular and extra cellular fluid. Deposition of fat and protein and increased cellular water are added to maternal stores. The average weight gain during pregnancy is 12.5 kg. During normal pregnancy 1 kg weight gain is due to protein. Also plasma albumin levels are

**Physiological changes pregnancy fig[5]**

Decreased and fibrinogen levels are increased. Total body fat increases during pregnancy. During second half of pregnancy plasma lipids increase but triglycerides, cholesterol and lipoproteins decrease soon after delivery. The ratio of LDL to HDL increases during pregnancy.

How a drug affects the fetus depends on the fetus’s stage of development and the strength and dose of the drug. Limited information exists regarding the effects of drugs in the period of
conception and implantation. It is suggested that women who are at the risk of conceiving or who wish to become pregnant should withdraw all unnecessary medications 3-6 months before conception. Certain drugs taken early in pregnancy (15-21 days after fertilization) during the period of blastogenesis may act in an all or nothing fashion; killing the foetus or not affecting it at all. During this early stage the fetus is highly resistant to birth defects. The fetus is highly vulnerable to birth defects between 3rd week and 8th week after fertilization; which is the period of organogenesis. All major organs start developing during this period. Drugs reaching the fetus during this stage may cause a miscarriage, an obvious birth defect, or a permanent but subtle defect, that is noticed later in life. At 9th week the embryo is referred to as a fetus. Development during this time is primarily maturation and growth. Exposure to drugs during this period is not associated with major congenital malformations but they may alter the growth and function of normally formed organs and tissues.

Concurrent use of other common medications during pregnancy such as antacids, iron and vitamins could also bind and inactivate some drugs. Intramuscular absorption of drug is generally more rapid due to increased blood flow; which enhances systemic drug absorption and the rate of onset of action. Lastly estrogen and progesterone alter hepatic enzyme activity; which can increase drug accumulation or decrease elimination of some drugs.[3]

Drugs categories in pregnancy

Drugs are teratogenic only at specific times during embryogenesis. Teratogenicity is a condition when any drug of chemical substance which produce deviations or abnormalities in the development of embryo. Therefore to avoid such problems it is very important to know which drugs should be prescribed during pregnancy. Food and drug administration (1979) of America enforce the rule for the categorization of the drug that is contraindicated during pregnancy so a classification has been carried out as following. The FDA has categorized the potential teratogenic risk of medications by an A, B, C, D, X system.

Category A

Controlled studies in women have failed to demonstrate a risk to the fetus in the first trimester and there is no evidence of risk in later trimesters. The possibility of fetal harm appears remote. Medications in this class are considered safe to use in pregnancy. Examples of medications in this class are vitamins and levothyroxine.

Category B
Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal studies have demonstrated risk to the fetus that was not confirmed in controlled studies in pregnant women in the first trimester and there is no evidence of a risk in later trimesters. Medications in this class are generally considered safe. Examples of medications in this class are acetaminophen and amoxicillin.

**Category C**
Studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women, or studies in women and animals are not available. Drugs from this class can be given to pregnant women if the benefit to the mother outweighs the risk to the fetus. Examples of medications in this class are diltiazem and spironolactone.

**Category D**
Evidence of human fetal risk has been documented, but the benefits to the mother may be acceptable despite the risk to the fetus. Drugs in this class may be used in pregnancy if the benefits to the mother outweigh the risk to the fetus (i.e., a life threatening situation or a serious disease for which safer medication cannot be used or are not efficacious). Examples of medications in this class are phenytoin and valproic acid.

**Category X**
Studies in animals or humans have demonstrated teratogenic effects. The risk to the fetus clearly outweighs any potential benefit to the mother. Drugs in this category are contraindicated in pregnancy. Examples of medications in this class are thalidomide and warfarin.\(^4\)

**How drug affect in pregnancy**
Drugs that a pregnant woman takes can affect the fetus in several ways. They can act directly on the fetus causing damage or abnormal development leading to birth defects or death. They can also alter the function of the placenta usually by constricting blood vessels and reducing the blood supply of oxygen and nutrients to the fetus from the mother and thus resulting in a baby that is underweight and underdeveloped. They can cause the muscles of the uterus to contract forcefully; indirectly injuring the fetus by reducing the blood supply or triggering pre-term labor and delivery.\(^3\)

**CONCLUSIONS**
The safe and unsafe medications during pregnancy is a very important prospective of life as it carries the two lives conjoined for the certain period of time. During that time period both the mother and fetus should be safe, sound and grow healthily. This review summarizes the safe and unsafe list of drugs during pregnancy it is the responsibility of all clinicians including pharmacists to counsel patients with complete, accurate and current information on the risks and benefits of using medications during pregnancy during the pregnancy as there are so many complications in it. It is the important that the benefits and risk of stopping treatment to be explained and informed properly. Drug may also be less effective during pregnancy because of pharmacokinetic changes such as increased metabolism. Doses of these drugs may need to be adjusting during pregnancy. Also when selecting drugs to be used in pregnancy effectively, drugs that have been in use for a long time are often preferable because fetal safety has been established even through newer alternatives may be available.\cite{4}

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