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Report on Teratogenic Agent and Drugs used in Pregnancy

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Abstract: *The physiology of pregnancy influences the pharmacokinetics of drugs taken, and some medications can reach the fetus and cause harm. This makes pregnancy a unique physiological condition for which drug treatment presents a unique concern. Pregnancy is not preventable completely and may even pose a risk if a woman has a medical condition that needs to be treated intermittently or continuously, such as asthma, epilepsy, or hypertension. Additionally, during pregnancy, preexisting medical conditions (such as migraines and headache) can worsen or generate new ones requiring for pharmaceutical treatment. One of the traditional issues in the field of medicine is the risk that certain medications taken when pregnant could harm the fetus. Phocomalia was a birth defect that was caused by pregnant women who consumed thalidomide in the 1960s. There are numerous further documented cases of teratogenic medication effects. Research has shown that barely one percent of all congenital defects are brought on by human teratogenic drug usage. In order to assess the teratogenic risk of pharmaceuticals, the Food and Drug Administration, or FDA, created a system in 1979 that takes the caliber of data from research including both humans and animals into account. The FDA divides all medications taken during pregnancy into five groups: A, B, C, D, and X. Pregnancy is not suggested in any circumstance when using category X products; category A is thought to be the safest category. This gives the clinician therapeutic direction. Numerous facets of drug usage during pregnancy are the subject of this essay.*

Keywords: radiation ,ionizing agents, teratogen

I. INTRODUCTION

The word "teratology," which comes from the Greek word "teras," which means "monster," has historically been used to describe the study of birth defects brought on by exposure to substances like lead, mercury, and other complicated compounds. The Greek word "monster" was originally used to describe severe physical deformities, but more recently, the term has also been used to describe deformities brought on by exposure to substances like lead, mercury, or other substances... Riley and Voorhees provided the most lucid explanation of the idea when it came to behavioral teratology during the 1960s and 1980s. The fundamental features of this extension are twofold. Firstly, behavioural abnormalities rather than physical defects are the main focus. Recognizing that many behavioral abnormalities may be mild in origin and not noticeable at all developmental stages is the second, and possibly more significant, step. Toxicology is closely related to the field of behavioural teratology. The majority of the time, behavioral teratology concentrates on behavioral abnormalities linked to known or suspected prenatal exposure to a possible toxin.

HISTORY

Teratology was first recognized in the 1930s when so many pigs became pregnant during the tests. Pigs used in these investigations were fed a diet lacking in vitamin A. All of those swine eventually developed fatal deviations, the most prevalent of which was the demise of their sight.

The human strain of rubella virus was initially recognized as a teratogene in 1941 and was discovered by Sir Norman Gregg. (1) As research into exotic food substances has advanced, animal testing have demonstrated their effects on embryos. Congeners of physiologically abundant compounds were utilized in these trials; these are most likely an amino acid counterpart of azaserine. Aminopterin was used to end the pregnancy in the 1930s. Instead, when the drug

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Conceptus development stage-

Organisms display varying levels of susceptibility to external stimuli based on their gestational age. During the initial three weeks of gestation, the conceptus is a fertilized egg cell. Following this period, the embryonic phase extends from the third to the eighth week, with the fetal phase coming afterward. Figure 2 illustrates the critical gestational phases.(4)

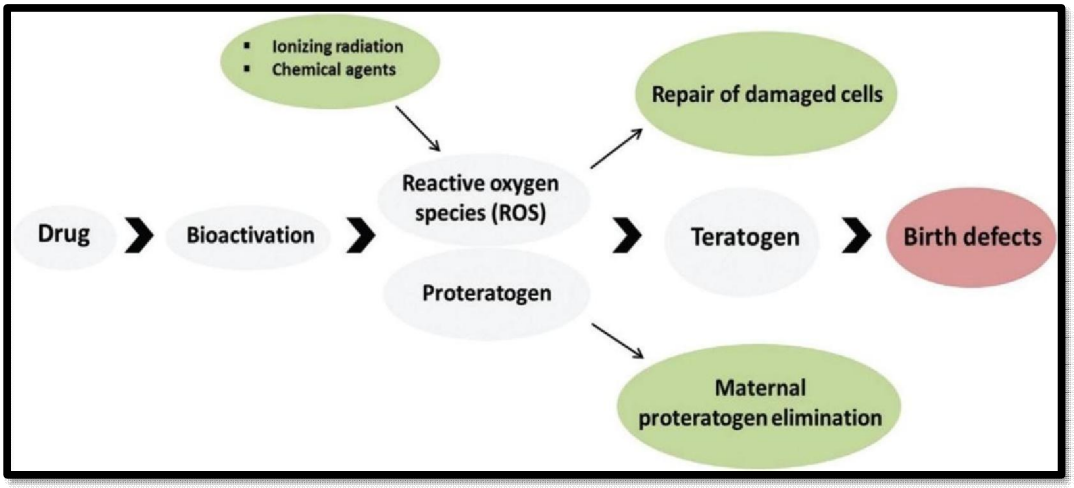

Figure 1:Teratogenesis pathways due to oxidative stress

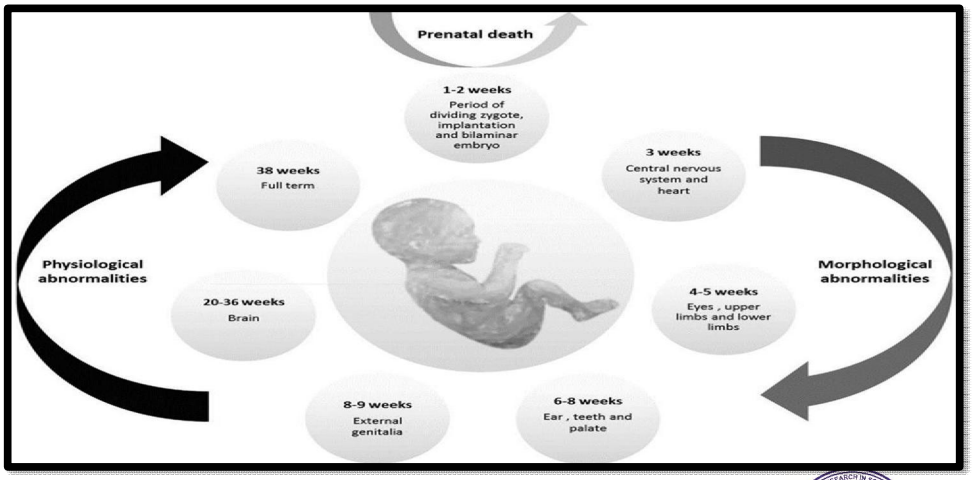

Figure 2. Critical stages of human embryo logical development

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The "all-or-nothing" phase, which lasts for the first two weeks after fertilization, is when a teratogenic factor can either cause a spontaneous abortion or normal embryo-fetal development. If teratogenic exposure occurs between the third and eighth weeks of gestation, when most morphological traits develop, it can result in significant phenotypic alterations in the embryo, including changes to the central nervous system, limbs, and face. After the ninth week of pregnancy, the brain and external genitalia are still growing organs, and exposure to teratogens can cause functional abnormalities in these organs. But going forward, the bulk of morphological characteristics are kept.(5)

Natures of the agent -

Teratogenic drugs can impact the developing embryo in diverse ways, influenced by their inherent characteristics. Ionizing radiation stands out as a physical teratogen with immediate effects on developing embryos. Conversely, medications and other substances undergo metabolic breakdown within the mother's body before reaching the fetus. Varied teratogenic susceptibilities can arise from the capacity of this metabolism to either activate or deactivate crucial metabolites.(6)

General mode of action of teratogen-

Determining the kind and degree of damage depends critically on when the teratogenic insult occurs in relation to fetal development. Organogenesis, histogenesis, and functional maturation are the three basic stages of mammalian fetal development. Ethanol is one of the teratogens that affects development at this incredibly early period.(7) Many teratogens have the capacity to halt cell division and kill embryo during cell division, which was implicated in blastocyst development. However, most of the time the embryo survives and seems to have little effect on its later development.(8)

When teratogens are injected between Days 17 and 60 of organogenesis, severe defects result. The organization of the embryo includes the bones and limbs, heart and main blood vessels, palate, genitourinary system, eye, and brain. Depending on when a teratogen is introduced, different malformations might result. For example, vitamin A derivatives, or retinanoids, are potent teratogens and essential for morphogenesis; yet, the cellular processes behind teratogens and their effects remain poorly understood. As a result, these compounds may have mutagenic consequences. Drugs like phenytoin and methotrexate alter the way that folate is metabolized, but they don't directly affect DNA.(9)

The development of the fetus is regulated by several hormones and is reliant on an adequate supply of nutrients throughout the later stages of histogenesis and functional maturation.

Exposure to mutants does not currently lead to the emergence of pronounced morphological abnormalities, even though teratogens affecting nutrient availability or hormone balance can potentially impede an organism's growth.(10) Fetal exposure to androgens may result in the development of masculine traits. In the 1950s, expectant mothers experiencing recurrent miscarriages with unclear causes were often prescribed stilbestrol. This medication led to dysplasia in the infant's vagina and elevated the likelihood of vaginal cancer in women during their teenage and early twenties.(11)

Drugs and Birth Defects -

When analyzing the potential therapeutic applications of pharmaceutical teratogens, it is important to take into account the larger context of human developmental disorders. Defects may occur for genetic, environmental, or other reasons. 25% are thought to have a genetic origin (Mendelian chromosomal, for example).(12) Over sixty-five percent of anomalies have unknown origins, although they most likely stem from a combination of genetic and environmental factors.It is important to do a comparative analysis between the likelihood of malformation subsequent to pharmaceutical exposure and the background rate, which is commonly documented as 2-3% for severe abnormalities in the general population.(13) A major malformation is one that requires considerable surgery for treatment (e.g., cleft palate or congenital heart disease), results in severe disability (e.g., mental retardation), or is incompatible with survival (e.g., anencephaly).If fine detail is examined for even little flaws like fingers or car registration plates, the percentage may rise to 7–10%. There is a maximum of 2-3% chance of congenital malformations as a result of drug exposure.(14) There is a chance that almost anything a pregnant woman eats might cause structural abnormalities or teratogenic consequences in the growing fetus. Lipid-soluble substances have an easier time passing across the placental barrier, while smaller molecular weight substances dissolve

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more quickly in water. (15)The quantity of medicine that can pass through the placenta freely is also influenced by how much a drug binds to plasma proteins.

The majority of drugs generally pass through the placenta to some extent, with the exception of large organic ions like insulin .(16)

Drug interaction mechanism:

i. Pharmacokinetic

ii. Pharmacodynamic

Interaction of Pharmacokinetic-

These interactions change the item drag's concentration at the location where it affects the object's distribution, metabolism, excretion, or absorption.

Absorption-

One typical feature of bioavailability is the movement of a medication from the place of delivery into the systemic circulation. Drugs reach 100% accessibility when they are injected intravenously, directly into the bloodstream. One important consideration is the amount or proportion of the active drug that stays in the systemic circulation.

One way to counteract this decrease in absorption is to provide two drugs, like tetracycline and calcium/ion salts, two to three hours apart.

During the first trimester of pregnancy, nausea and vomiting may reduce the quantity of medicine that is absorbed.

Furthermore, pregnancy raises the pH of the stomach by decreasing the generation of gastric acid and increasing the release of mucus.

Distribution-

Medication can be moved back and forth between different sites after it has entered the systemic circulation. The volume of distribution indicates how much of a systemic dosage of medication is finally dispersed throughout the body because the first medication is removed from its binding sites on the plasma protein by another medication.

EG. Digoxin combined with quinidine

Metabolism-

Using specific enzymatic systems, drugs are chemically modified during drug metabolism. Metabolism causes certain drugs that are delivered as inactive pro-drugs to lose their pharmacological action. The bulk of medication metabolism occurs in the liver.

Some medications either increase or decrease the rate at which other drugs are metabolized.

For instance, rifampicin and barbiturate, which increase microsomal enzymes, might lead to the failure of contraceptives.

Excretion-

Tubular secretion, reabsorption, and glomerular filtration rate (GFR) all affect how much medication is excreted from the kidneys. GFR increases by 50% by the first trimester and continues to climb until the last week of pregnancy. When a medicine is removed predominantly by glomerular filtration, alterations in GFR during pregnancy are likely to influence the drug's renal clearance. For instance, there is an increased renal clearance of medications such as clindamycin and cefazolin during pregnancy.

Although GFR rises steadily during pregnancy, differences in renal tubular transport may have distinct consequences on medications that the kidneys are able to eliminate.

Crucial for medications that are actively secreted through tubular transport mechanisms.

For example, probenecid prolongs the plasma half-life of cephalosporin and penicillin by inhibiting their tubular secretion.

Pharmacodynamic Interaction-

These interactions occur when a medication, regardless of concentration changes, alters the way another medicine acts at the target site.

This may result in:- Enhanced response, known as synergism.

weakened reaction known as antagonism.

Unusual reaction, indicating direct impact on each other's consequences.

When medications directly affect one another's effects, this is known as a pharmacodynamic interaction.

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Often, a pharmacodynamic interaction is purposefully sought for, especially when looking for mutually reinforcing effects in the same direction, as shown in the use of anti-infective medicines or in pain management.

Pharmacodynamics is regulated by elements like as receptor binding and sensitivity, post-receptor effects, and chemical interactions.

Moreover:

When two medications act on the same receptor, this is known as additive behavior, and the total impact of the two medications is their sum, up to their maximum effect.

One kind of synergism known as potentiation occurs when a medication can increase the effects of another medication while having no impact on its own.(17)

Typical teratogens in humans include: Medicines-

The ACE inhibitors captopril, enalapril, and benazepril
Diclofenac is a nonsteroidal anti-inflammatory drug
Estrogens are androgen hormones.
Antiepileptic drugs:
trimethadione, phenytoin, valproic acid, and carbamazepine
Anti-tumor agents: aminopterin and methotrexate
Xanthine Warfarin Alkaloids:
Coffee,Chemical pesticides:
Herbicides with organophosphates:
Mustard with sulfur and glyphosate
Superfluous chemicals:
Cocaine and alcohol
Other substances:
Mercury methyl
Ionizing radiations:
Cigarette smoke
Physical agents:
high dosages exceeding 5 rad.
Biological agents, such as infections in fetuses:
Rubella Cytomegalovirus □
Diseases of mothers:
Diabetes ID, epilepsy
Phytochemicals:
Cyclopamine, an alkaloid found in veratrum
Other agents:
Carrageenan lambda (18)

Fig 3: common human teratogens

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Drugs-

Penicillamine-

D-penicillamine (DPA) (dimethyl cysteine), an amino acid that contains sulfhydryl groups, can chelate metals, particularly copper, and accelerate the metal's excretion from the body. There is a drop in tissue copper content with increased dosing. Several studies have revealed that DPA-treated pregnant women had malformations in their fetuses.(19) Copper may have a mediating role in the emergence of fetal abnormalities, according to a relationship between low copper levels and a high frequency of congenital malformations and mortality.

Due to its ability to cross the placental barrier, DPA may have teratogenic effects. Pregnant women treated with DPA had infants with serious connective tissue defects.(20)

abnormalities For conditions like Wilson's disease, rheumatoid arthritis, and cystinuria—all of which have major teratogenic consequences on expecting mothers—it is the advised course of treatment. For this to occur, the collagen and elastic fibers in the dermis need to be cross-linked. Lysyl oxidase is an enzyme that depends on copper. The depletion of copper from tissues caused by penicillamine's indirect reduction of enzyme activity results in the formation of abnormal elastic fibers.

Moreover, the drug inhibits lysine residue deamination, which contributes to the aberrant accumulation of elastic fibers and is required for the development of collagen and elastin.(21)

Thalidomide-

The most well-known teratogen in medical history is thalidomide. Even at relatively low dosages, thalidomide causes the growing fetus to acquire severe limb abnormalities. Thalidomide produces limb abnormalities such as phocomelia and amelia, which are characterized by significant shortening or full elimination of legs and/or arms; ear malformations include anotia, microtia, and hearing loss.(22)

Through abnormal nuclear Factor-kB activation, thalidomide can cause oxidative stress and reactive oxygen species, which in turn can enhance the production of proteins that are important for bone morphogenicity. This mutation stops the synthesis of signaling proteins, protein kinase B, and fibroblast growth factor (Fgf8/Fgf10), which are all necessary for cell survival and proliferation. Thalidomide consumption during the first trimester of pregnancy induces organ dysgenesis.

Thalidomide's antiangiogenic impact inhibits the production of long bones in the embryonic body and causes cell death and downregulation of growth factors such as Fgf8 or Fgf10. One of the reasons cells die is because growth factor signaling pathways become interfered with. Mesenchymal loss and limb abnormalities are the results of this sequence of events[25, 27]. It produces free radicals that cause teratogenic effects and damage to the cellular macromolecules of developing organisms.(23)

Thalidomide has been seen to cause damage to DNA, produce reactive oxygen species, and accumulate 8-hydroxy20-deoxyguanosine in rabbits. Cereblon is a protein that we have discovered binds to thalidomide. The drug binds to retinol, the main target of thalidomide teratogenicity, reducing its action.(24)

Warfarin-

Rats and mice suffer internal bleeding as a result of its potent natural coumarin's rodenticide effects. It is now present in the field of clinical medicine as well. Warfarin's water solubility, oral bioavailability, and reversibility are advantageous when combined with vitamin therapy. Warfarin and fetal malformations are related.(25)

It causes embryo toxicity during the first six to nine weeks of pregnancy. Pregnancy-related warfarin use has been connected to distal limb hypoplasia, spontaneous miscarriage, stillbirth, nose hypoplasia, stippled epiphyses, and abnormalities of the CNS, eye, jaw, and urinarysystem.Infants born to mothers typically suffer from CNS abnormalities and neurological illnesses mostly due to microhemorrhages in neuronal tissue caused by insufficient vitamin K stores .(26)

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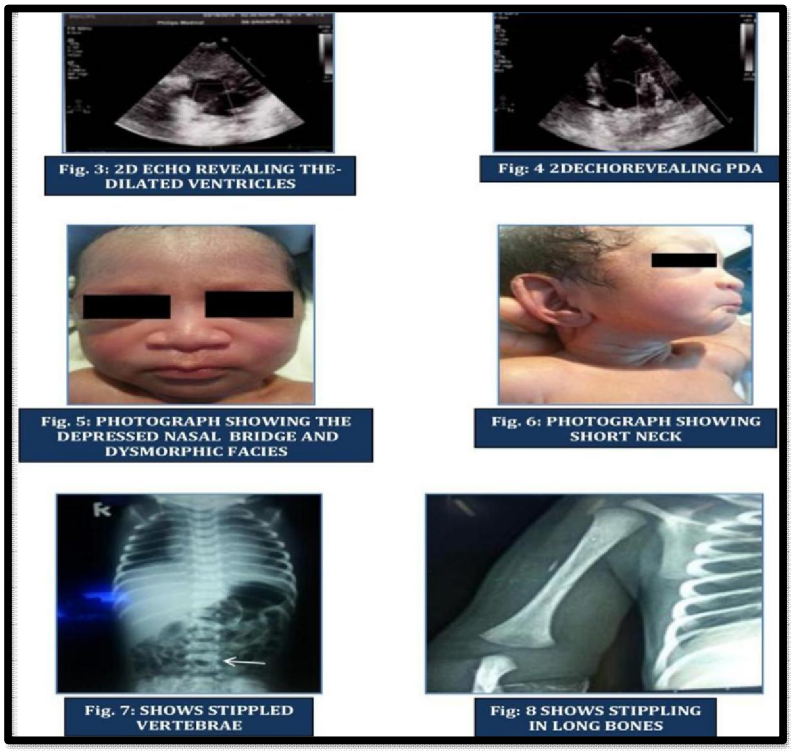

Fig4:-Fetal Warfarin Syndrome

Unnecessary chemicals

Spirits: -

A 1973 study report on the teratogenic consequences of alcohol drinking was the first to mention fetal alcohol syndrome (FAS). The term "FAS" refers to a pattern of birth abnormalities in infants whose parents consume large amounts of alcohol. Children with FAS frequently exhibit abnormalities of the brain, limbs, and craniofacial structure in addition to a high risk of developmental delays. The majority of alcohol teratogenicity instances included children born to pregnant women who drank a lot of alcohol. A multitude of variables, such as genetic traits inherited from the father or mother, may influence the fetus's vulnerability to alcohol-related harm. It is thought that a father's alcohol consumption may change the fetus's genetic makeup, create new sources of variability.

Alcohol easily passes through the placental barrier. The main cause of FAS is the ability of alcohol and/or one or more of its metabolites, such as acetaldehyde, to cross the placenta. Alcohol accumulates in amniotic fluid, which serves as a reservoir for unmodified alcohol and acetaldehyde due to the dynamics of amniotic fluid circulation and the lack or very low amounts of the enzymes necessary for drug biotransformation during fetal development. As a result, both medications are administered to the unborn foetus long after it has left the mother's body.(27)

COCAINE-

Cocaine is one of the most strong psychoactive drugs. Because it can restrict sodium ion permeability and inhibit catecholamines, dopamine, and tryptophan from being reabsorbed post-synaptically, it has anesthetic effects. Both benzoylecgonine and its metabolite, benzoylnorecgonine, has strong pharmacological effects and are neurotoxic. The medication may cross the placental barrier on its own and through its metabolites, which accounts for its strong effects on fetal development. The effects of cocaine on a mother's cardiovascular and autonomic systems might indirectly affect the development of the fetus. Cocaine usage during the first trimester may raise the risk of structural abnormalities because of its strong vasoconstrictive effects. One of the primary causes of maternal morbidity and fetal mortality, placental abruption, was observed in the women undergoing cocaine therapy. Placental abruption is the term for an early separation of the placenta, which is normally implanted. This may be the result of the medication-induced hypertension in the mother.

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A dose-dependent initial decrease in uterine blood flow occurs when cocaine is administered to pregnant sheep. As a result, the fetal body's tissues are destroyed, the fetal arterial partial pressure drops, and organ deformity results. (28)

Other chemicals-

Methylmercury-

It is generally established that methylmercury exhibits a number of toxicities, such as those of a teratogen, neurotoxic, and endocrine disruptor. Methylmercury exposure alters the behavior and health of both humans and wildlife.

Eating seafood that has been contaminated with methylmercury is frequently the source of exposure. Overexposure to chemicals during pregnancy can cause severe mental impairment and neurobehavioral abnormalities, such as cerebral palsy. Additionally, it is linked to low birth weight and early sensorimotor impairments, such as a delayed start to walking. Exposure studies on rats and nonhuman primates revealed alterations in their neurobehavior. It also has neurotoxic effects on a fetus's and a child's development. It is recommended that expectant mothers and women nearing childbirth refrain from being exposed to methylmercury in order to prevent these teratogenic exposures.(29)

Leadacetate-

Lead is a common problem in public and occupational health that has several detrimental effects on males and females alike. A previous study using experiments revealed nephrotoxicity from lead. Exposure to large dosages affects the reproductive systems of both men and women.

The frequency of miscarriages and stillbirths increases among women exposed to lead. Serious effects of lead exposure include an increase in the frequency of irregular menstruation, spontaneous abortions, and threats of abortion.

Oral treatment of lead acetate was reported to halt the development and maturation of ovarian follicles in mice. Furthermore, it causes abnormal spermatozoa morphology in male offspring mice, harming the sperm. It has the effect of producing anomalies in the sertoli cells because it interferes with their metabolic activities.(30)

Physicalagents-

Cigarette smoking-

One of the main risk factors for general developmental abnormalities is mothers who smoke. The fetus is growing at a slower rate. A variety of substances, including carbon monoxide, nicotine, and nicotine generated during smoking, prevent amino acids from crossing the placenta. While the precise mechanism responsible for producing teratogenic consequences in humans remains unclear, several processes have been suggested, such as placental necrosis, placental exchange obstruction, and the activation of hazardous reactive metabolites that rely on metabolic enzymes.

Due to the fact that carboxyhemoglobin has a longer half-life in fetal blood than in maternal blood, smoking-related carbon monoxide increases blood levels and crosses the placenta.

Uterine vascular constriction and intrauterine growth retardation result from nicotine's vasoconstriction effect, which lowers the perfusion of embryonic tissues. Moreover, it increases the risk of perinatal death and morbidity. Perinatal mortality is associated with a number of conditions, including preterm delivery, premature birth, intrauterine growth retardation, subfertility, abnormal placentation, childhood morbidity and mortality, congenital malformations, gastroschisis, cardiac defects, chromosomal abnormalities, and central nervous system defects.(31)

Maternal Disease -

Diabetes-

Congenital abnormalities, which are more common in the children of mothers with insulin-dependent diabetes, are the primary cause of perinatal death in these newborns.

The underlying mechanisms of these consequences are not fully understood. The metabolic alterations brought on by diabetes lead to an increase in the production of basement membrane constituents, which are essential for morphogenesis. A prior study in rats found that maternal diabetes preferentially alters gene expression in the developing rat embryo. These adjustments include substances (extracellular matrix components) that are essential for morphogenesis. Changes in associated proteins and mRNA were also found. Changes in the distribution and activity of the protein kinase C isoform were seen in the embryos of diabetic rats.

Rats suffer teratogenic effects when hypoglycemia is prevalent during the early stages of organogenesis.(32)

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FDA Categories for drug use in pregnancy-

The food and drug administration is in charge of ensuring the safety, efficacy, and security of pharmaceuticals for use in humans and animals as well as biological products, medical devices, food supplies, cosmetics, and items that emit radiation. All of these things contribute to the public's health.

In order to evaluate the teratogenic risk of medications, the Food and Drug Administration established a procedure in 1979 that considers the quality of evidence from studies involving both people and animals. It provides guidance on therapy for the health care provider. Although several medications from groups B, C, and D are also used during pregnancy, category A is thought to be the safest. The only classification that indicates a medicine is completely not recommended for usage during pregnancy is Category X. The following table lists some of the medications that are often taken during pregnancy along with their classifications (as determined by the FDA categorization).(34)

Drugs	Category
Analgesics and Antipyretics	B and C
Acetaminophen	B
Phenacetin	B
Aspirin	C
Antiemetics	B and C
Doxylamine	B
Meclizine	B
Cyclizing	B
Dimenhydrinate	B
Antibiotics	B and C, D
Penicillin, ampicillin, Amoxycillin	B
Cloxacillin, cephalosporin	B
Erythromycin	B
Gentamicin	C
Amikacin	C/D
Streptomycin	D
Sulphonamides	B/D
Tetracycline's	B
Amoebicides	B
Anthelmentics	B
Antimalarials	C
Antifungals	C
AntiTBDrugs	B and C
Ethambutol	B
INH	C
Rifampicin	C
Pyrazinamide	C
PAS	C
Vit. B, C, D, E, folic acid	A
Thyroxin	A
Androgens	X
Oestrogens	X
Progestogens-Hydroxyprogesterone	D
Medroxyprogesterone	D
Norethindrone	X

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Bronchodilators	X
Norgestrel	C

Case Report -

A 19-year-old patient diagnosed with gravida 1 para 0 was referred for amenorrhea lasting seven weeks and six days. Since learning that the patient had CML a year earlier, the patient had been taking 200 mg of radotinib twice a day.

orally each day for a whole year. Six months before referral, in the chronic phase, a complete cytogenic response was established. The patient had a regular menstrual cycle.The urine sample tested positive for human chorionic gonadotropin (HCG), and the ultrasound measurement showed that Gsac was 1.26 cm. At five weeks and five days of gestation, the fetal pole had a measurement of 2.4 mm. The fetus's heart rate was 105 beats per minute. Concerned about the teratogenic implications of radotinib, she decided to terminate her pregnancy.The patient went back to the hospital for a further 11 weeks and 4 days of amenorrhea three years later, at the age of 22. Her periods were normally regular. The patient was taking 300 mg of radotinib orally twice a day at that point. However, the patient had stopped taking radotinib 12 days before to this appointment when a positive urine HCG test resulted.During an ultrasound scan, a single intrauterine pregnancy measuring 12 weeks and 3 days of gestation was found. It was hypothesized that she used radotinib up to 10 weeks and 5 days into her pregnancy.(35)

The woman made the decision to continue her pregnancy and stopped taking radotinib. The blood study's findings revealed that the white blood cell count was 5,490 cells/mm3, the hemoglobin level was 9.4 g/dl, and the platelet count was 64,000 cells/mm3. Her kidneys and liver were both functioning normally. The expecting woman had standard prenatal treatment; no significant results were observed. She got a complete blood count every month. There was no medical opinion that CML was getting worse.

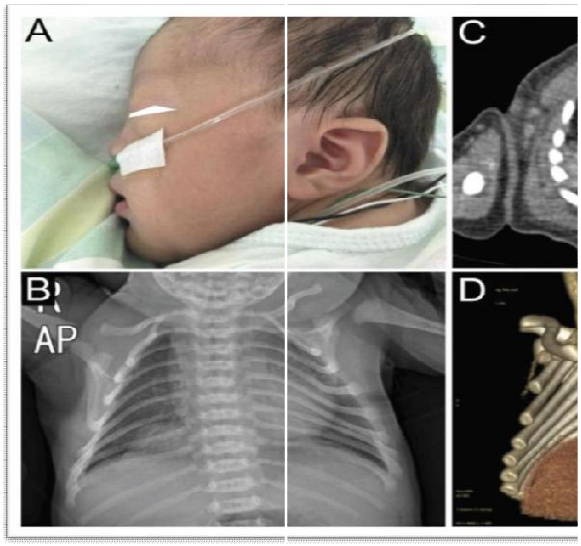

Fig5.1a,1b,1c,1d

On the 39th week and 6th day of pregnancy, the patient gave birth to a daughter weighing 3.330 kg vaginally. The infant had an 8 at one minute and a 9 at five minutes on the Apgar scale. A thorough examination revealed low-set ears as well as an absence of a forehead-to-nose angle (Figure 1A). No more extrinsic distortion was found. But when the patient was breastfeeding, the baby's cowish weeping was accompanied by cyanosis and almost 70% desaturation. An x-ray of the chest revealed both lower lungs to be hazy. A potential rib deformity was detected (Figure 1B). A CT scan of the chest revealed atelectasis in both lower lungs (Figure 1C).It was determined that the rib cage was normal, as shown in Figure 1D. On the echocardiogram, there was nothing interesting to mention. Laryngoscopy was used to detect laryngomalacia. The arytenoid compressed and the omega-shaped epiglottis expanded during inspiration. During placental pathological examination, increased intervillous fibrin deposition was seen; no other anomalies were discovered. The baby's desaturation and atelectasis improved by the time she was 10 days old. As a result, she was

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allowed to leave the hospital. At the three-month mark, the results of the follow-up visit showed no additional abnormalities.

In conclusion, women of childbearing age should learn about contraception before becoming pregnant, as radotinib has been demonstrated to have teratogenic consequences.(36)

II. CONCLUSION

- Knowing the process behind the induction of birth defects Is Essential for ascertaining How to avoid these consequences
- Enhancing the precision of experimental animal extrapolation would facilitate the analysis of experimental results to ascertain the likelihood of a particular substance causing birth abnormalities in humans.
- Select the right medication and limit needless exposure.
- Before beginning treatment, educate the patient.
- Risk-benefit evaluation

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