

## Drugs that cause fetal abnormalities

Hamza Khalifa Ibrahim<sup>1\*</sup>, Noor-Alhooda Milood Al-Awkally<sup>2</sup>, Abeer Makhlof<sup>3</sup>, Amina Farag<sup>4</sup>,  
Seham Miftah<sup>5</sup>, Marwa Salih<sup>6</sup>

<sup>1,3,4,5,6</sup>Higher Institute of Medical technology, Bani Waleed, , Libya

<sup>2</sup>Medical Laboratory Department, Higher Institute of Science and Technology, Sulug- Libya

Corresponding Author: [hamzakhelifa2009@gmail.com](mailto:hamzakhelifa2009@gmail.com)

### ABSTRACT

*The degree of occurrence of fetal deformities ranges based on the level at which the fetus is subjected to environmental stimuli or genetic factors., and the many factors causing the abnormalities different tests to detect abnormalities, including those who detect the deformity in a period of easy abortion, including those that have been discovered late. Drugs are one of the most serious causes of fetal abnormalities because pregnant women have to use them, either because they are chronically ill or at some stage of pregnancy with a specific disease. The goal of the study is to explain some of the medications widely used by pregnant women whether these drugs are safe or causing fetal anomalies., and establish during what point these medications are considered to be healthy and at what stage they are considered skewed as certain drugs are considered safe at several months of pregnancy and corrupted at the rest of the months after they have been deformed at all periods of pregnancy.*

**Key words:** CI Fetal abnormalities; Defect from birth; Drugs

### INTRODUCTION

Pregnant women can experience temporary health problems during pregnancy, such as leaching, bronchitis, Pregnancy diabetes or elevated blood pressure. Pregnant women may have chronic diseases such as diabetes, pressure, rheumatism, and other diseases that require treatment and follow-up even during pregnancy. In addition, Pregnancies are associated with alarming signs like nausea, vomiting, constipation, dizziness and others.

In fact, these all signs and health issues need to be treated, especially during pregnancy, Although the continued suffering of the pregnant woman and the lack of control of infection will adversely affect the mother's health and the child and may lead to complications like abortion or the occurrence of defects or poor fetal development.

Any pregnant women are also anxious and concerned about the risk of fetal defects in the first

month of pregnancy and may believe that a certain diet or drug may affect their fetus because the incidence of fetal deformity has recently risen and it is no longer an uncommon occurrence.

There are some types of anomalies that can be detected early in the first three months that are common and occur as fetal organs are developed.

There are other types known after birth, especially abnormalities related to external appearance and others are not detected until after a period of birth are abnormalities related to physiology.

## MATERIAL AND METHODS

### Fetal Malformation

There are several causes that cause distortions, including:

#### Infection:

The infection that spreads may be caused by bacteria or viruses or, in rare cases, by parasites that are transmitted directly from the mother to the fetus during pregnancy or childbirth. It can occur when a mother is infected as a concurrent disease during pregnancy.

For example, rubella causes abnormalities in the eye, inner ear, heart, and sometimes tooth deformities. When the fetus is exposed to rubella between the fifth week. and the tenth week.

Mother's exposure to cytomegalovirus can lead to microcephaly, cerebral calcification, blindness, chorioretinitis, retinopathy, enlarged liver and fetal meningitis.<sup>[1]</sup>

Microcephaly, retinal dysplasia, and mental retardation may result from the Herpes virus.<sup>[2]</sup>

The sensitivity of moth The sensitivity of mothers to toxoplasmosis in children will cause brain calcification and mental retardation. ers to toxoplasmosis in children will cause brain calcification and mental retardation. Syphilis causes congenital deafness and mental retardation.<sup>[2]</sup>

#### Rays:

In the first trimester, exposure to varying radiation results in chromosomal anomalies, reduced development within and outside the uterus, and congenital malformations, often leading to fetal mortality, miscarriage, or birth defects.<sup>[3]</sup>

#### Alcohol abuse:

Studies have shown that children with Fetal Alcohol Syndrome are a result of the mother's abuse of alcohol. Persistent birth defects include: Brain injury, mental incapacity, heart problems, and skeletal anomalies are all examples of craniofacial abnormalities.<sup>[4]</sup>

#### Medicines and supplements:

The most famous deformity drug is thalidomide. It is prescribed to pregnant women as a means of stimulating sleep and Because of their capacity to prevent nausea, anti-emetic drugs are used, as taking this drug in the fifth and sixth weeks affects the formation of limbs and leads to birth without limbs.<sup>[5]</sup>

-Retinoic acid (vitamin A) Retinoic acid derivatives are used in the treatment of acne, but researchers have proved that it is strong deformed when taken orally. Retinoic acid can produce a wide range of defects, these include a variety of facial skeletal abnormalities, and outgoing tracts of

the heart.

- Tetracycline When used by pregnant women, this antibiotic causes a condition called tetracycline teeth that causes both have a faulty development dentin and tooth enamel and affects bone maturation.<sup>[5]</sup>

- Many anticonvulsants, such as phenytoin and carbamazepine, are known to cause severe disfigurement. This drugs induce what is called (Hydantoin syndrome in the fetus), and can usually involve a large nasal foundation, cleft lip, tiny endocrine, hypoplasia, and mental retardation. In addition to Valporic acid, which is also a widely used antiepileptic and when taken during pregnancy causes defects associated with the closure of the neural tube Spina bifida, such as.<sup>[5]</sup>

### **Hormones:**

Estrogen derivatives in addition to progesterone derivatives sometimes cause deformities of the spine, anus, heart, trachea and kidneys, “If these pills were taken especially during the first period of pregnancy”.

Diethylstilbestrol “This substance is a sex hormone derived from estrogen, and when taken by a pregnant woman, it causes tumors in the child's vagina as well as an elevated chance of ovarian cancer and adenomas in the reproductive system”. As well as males who have been exposed to this drug while in the womb of their mothers for some abnormalities in the composition and function of the urinary and reproductive system and often semen abnormal.<sup>[6]</sup>

-Methotrexate acts as an anti-folic acid important for cell division and is still widely used in medicine in the treatment of certain cancers and malignancies. “However, the use of this drug causes severe birth defects in the fetus if used by pregnant women because it affects the cells of the fetus and most of the abnormalities are in the spine, skull, face and limbs”.

### **Caffeine:**

“In tea, coffee and cola there is a stimulant. Some research has reported that a lot of them during pregnancy cause a decrease in the growth of fetus and therefore should not be a lot of these substances”.<sup>[5]</sup>

### **Nutrient deficiencies:**

For example, deficiency of folate and vitamin B9 in a mother's Spina bifida is caused by defects in the cellular neural tube.

Iodine deficiency in the diet of the pregnant mother may cause a deficiency of the thyroid gland of the fetus, which leads to mental and physical retardation, but is easily treated with thyroxine.<sup>[7]</sup>

### **Amniotic fluid:**

This fluid is formed in the early period of fetal growth, since the beginning of the second week and grows with the development of the fetus and surrounds the fetus to protect the fetus and protect it from shocks and movements experienced by the pregnant and therefore lack of amniotic fluid leads to the formation of a bundle adhere to the fetus and these bundles abound due to adhesion Thus external abnormalities are formed on the outside of the body.<sup>[7]</sup>

### **Smoking:**

Father smoking before pregnancy has been linked to an increased risk of birth defects in the

offspring due to the combination of carbon monoxide combined with hemoglobin (carboxyhemoglobin) so that the toxic substance that prevents hemoglobin from performing its function in the transfer of oxygen is optimized and leads to some deformation of oxygen. Congenital or underweight and small placenta size. Nicotine is an addictive substance in tobacco. This substance causes an increase in adrenaline and thus causes narrowing of the blood vessels feeding the placenta, thus reducing perfusion and nutrition of the fetus. Thiocyanate, which is found in cigarettes, seeps into the mother's blood and into the placenta and fetus, causing non-growth due to harmful effects.<sup>[18]</sup>

### **Parent's age:**

Some complications of childbirth can often occur due to the age of an advanced mother (older than 35 years), which includes restriction of fetal growth, Placental abruption and preeclampsia. Several studies have found a link between advanced parental age and the probability of birth abnormalities as parents contribute to a relatively greater DNA mutation such as limb abnormalities and Down syndrome, to a comparatively greater DNA mutation in their offspring.<sup>[8-9]</sup>

### **Diagnostics currently available**

#### **Ultrasound examination:**

This examination identifies very accurately diseases of the nervous system in the fetus such as neural tube defects, Tiny brain and heart abnormalities, such as a ventricular wall hole, and bone structure and limb defects, such as lack of limbs.

However, this test is not conducted to identify birth defects only in the second half of pregnancy, usually in the sixteenth to eighteenth week, and here the disadvantage of this method is that the diagnosis is made only the fetus has exceeded for 120 days, and therefore can't be allowed Abortion once the fetal deformity is proven.<sup>[10]</sup>



**Fig 1.** Ultrasound examination

#### **Fetal Endoscope:**

This endoscope is used in the uterus and later in the tuberculosis cavity to see that the fetus contributes to the detection of external morphological congenital malformations.

The placenta and the fetus are first identified by ultrasound and then enter a microtome. This test is performed around the 16th to 18th week.<sup>[1-3]</sup>

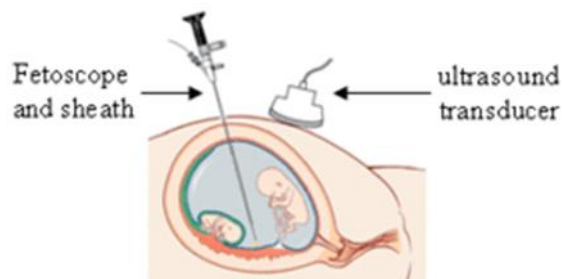


Fig2. Fetoscopy

### Alpha-pheto-protein:

It is a glycoprotein formed in the fetus during pregnancy, and is used to diagnose many congenital diseases of the fetus, and can also be used to predict the possibility of cancerous tumors such as hepatocellular carcinoma.

In pregnant women, alpha-phyto-protein is measured using either maternal blood or peri-fetal fluid when testing for abnormalities in fetal development. High rates of neural tube defects lead to Down syndrome. This analysis is carried out in the fourteenth week.<sup>[15]</sup>

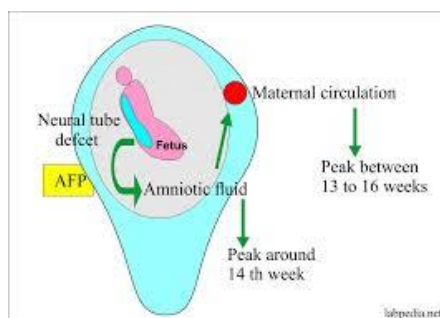


Fig 3. Alpha fetoprotein

### Withdrawal of amniotic fluid

This is usually done in the fifteenth or sixteenth week of pregnancy and the doctor withdraws about 10 millimeters for laboratory tests.

This test is difficult to perform before the 14th week because of a small amount of fluid. This test is used if the mother is 35 years of age or older, the birth of a deformed child, the presence of a chromosomal dysfunction of one of the parents, women with genetic diseases in the sexual chromosome x and defects of neural tube formation in the family.<sup>[16]</sup>

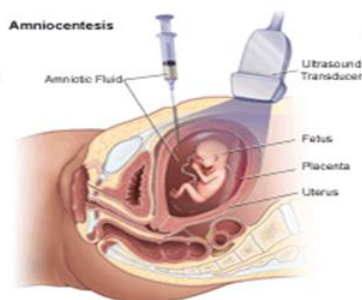
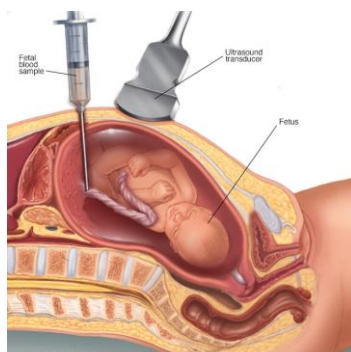


Fig 4. Amniocentesis

## Fetal blood test

A blood test is used to identify the many defects of hemoglobin, especially hemolytic anemia, known as thalassemia, and to identify some of the chromosomal defects that appear by examining the lymphocytes of the fetus.

Fetal blood testing is increasingly used to determine whether the fetus has infectious microbial diseases such as HIV, herpes virus and rubella virus.<sup>[17]</sup>



**Fig 5.** Chorionic Villus Sampling

## Use of medicines during pregnancy

The fact that some medications given during pregnancy may be harmful to an unborn baby is one of the classic problems in medical treatment. Pregnant mothers who obtained Thalidomide gave birth to children with Fukumalia in the 1960s. Other examples of the teratogenic effects of drugs include: it has been reported that birth defects caused by human teratogenic drugs account for less than 1% of overall birth defects, In 1979, the Food and Drug Administration developed a system for assessing the horrible risk of medications by taking into account the accuracy of results from animal and human studies.<sup>[18]</sup> The FDA categorizes numerous medicines used during pregnancy into five categories: (A), (B), (C), (D), and (E) (x). This gives the doctor therapeutic direction. This page discusses many elements of drug usage during pregnancy.

Tab 1. Drug classification by the FDA for use during pregnancy.

Category	Description
A	Adequate, all around controlled investigations in pregnant ladies have not demonstrated an expanded danger of fetal irregularities.(19)
B	Animal tests have found little signs of damage to the fetus, but in pregnant women there are no appropriate and well-controlled studies. Or on the other hand creature examines have demonstrated an antagonistic impact, yet fitting and very much controlled investigations of pregnant ladies have not indicated a danger to the fetus.(19)
C	Animal tests have shown adverse effects and there are no appropriate and well-controlled studies of pregnant women. Or no animal experiments have been performed and no appropriate and well-controlled studies have been conducted in pregnant women.(19)
D	Studies, satisfactory all around controlled or observational, in pregnant ladies have shown a

	danger to the embryo. Nonetheless, the advantages of treatment may exceed the expected danger.(19)
X	Studies, satisfactory all around controlled or observational, in creatures or pregnant ladies have shown positive proof of fetal anomalies. The utilization of the item is contraindicated in ladies who are or may get pregnant.(19)

Tab (2) Some drugs that cause birth defects

Drugs	Category of Pregnancy	Adverse effect	Period caused by deformities	Pregnant women may use it in case
Chloramphenicol	C	It causes gray baby syndrome, which is a symptom of general weakness, pale gray skin, hypotension, cyanosis, hypotension, vomiting, refusal of the baby to feed, flatulence, irregular breathing may result in death within hours.	Do not use in 3 <sup>rd</sup> trimester of pregnancy.	Probably uses for meningitis.(15)
Tetracycline	D	It causes staining of the fetal teeth brown and affects their growth and bone growth.	In 2 <sup>nd</sup> trimester, 3 <sup>rd</sup> trimester. Specifically from 16 <sup>th</sup> week of pregnancy.	Probably uses for treatment acne.(11)
Gentamicin	D	It causes ototoxicity that leads to hearing loss as well as kidney damage to the fetus.	Do not use in pregnancy unless it is the only option of treatment.	Probably uses in the treatment of respiratory tract infections.(13)
Trimethoprim /Sulfamethoxazole	D	It causes neural tube abnormalities. Structural defects and cardiac abnormalities.	Do not use in all trimesters of pregnancy. Unless no other treatment is available.	Uses for treatment of acute pneumonia.(1-2)

**Tab (3)** Drug classification by the FDA for use during pregnancy

Drugs	Category of pregnancy	Adverse effect	Period caused by deformities	Pregnant women may use it in case
Ciprofloxacin (22)	C	It causes osteoathopaty.	In 2 <sup>nd</sup> trimester,3 <sup>rd</sup> trimester of pregnancy.	Uses for treatment of urinary tract infection.(17).(21)
Acetylsalisalic acid	D	it causes early closure of the arterial canal Leading to high blood pressure, pulmonary failure and right ventricular failure.	In 2 <sup>nd</sup> trimester,3 <sup>rd</sup> trimester of pregnancy.	Used to increase the blood supply of the fetus from which oxygen and food are (17).derived
Warfarin	X	In 1 <sup>st</sup> trimester causes warfarin fetal syndrome ,in 2 <sup>nd</sup> trimester and 3 <sup>rd</sup> trimester causes defects of the central nervous system and defects in kind.	Do not use in all trimesters of pregnancy.	Uses for treat blood clots such as deep vein thrombosis ,pulmonary embolism.(4)
Lisinopril	D	It causes an imbalance in The formation of renal tubules and low fetal blood pressure.	Not recommended during the 1 <sup>st</sup> trimester and use is contraindicated during the 2 <sup>nd</sup> and 3 <sup>rd</sup> trimesters.	Uses in cases of severe hypertension.(1)
Atorvastatin	X	It causes structural and genital abnormalities.	Do not use in all trimesters of pregnancy.	Uses if cholesterol is higher than normal.(2)
Prednisolone	C	It causes cleft palate.	In 1 <sup>st</sup> trimester of pregnancy.	used to treat many inflammatory such as arthritis, psoriasis.(11)
Estrogen	X	It causes vaginal cancer.	Do not use in all trimesters of pregnancy.	You may use it to prevent pregnancy.(7)

### CONCLUSION

The particular nature of pregnancy physiology provides obstacles for pharmacological treatment of chronic and acute diseases, as well as symptom management of numerous pregnancy-related ailments. All physicians, including pharmacists, are responsible for providing patients with comprehensive, accurate, and up-to-date information about the risks and benefits of using drugs during pregnancy. Prompting ladies who have been presented to prescriptions on the danger of teratogens incorporates characterizing the portion effectively and measuring the seriousness of the presentation. For physician endorsed prescriptions, this might be simple, however for ethanol or



other illegal substances or OTC medications, it could be significantly more confounded.

“We therefore recommend that treatment during pregnancy be further investigated in future case-control studies to fully

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