



The Overview on Cancer during pregnancy

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1. Abstract :

The number of women is suffered from cancer during pregnancy. It's extremely harmful to the baby and foetus. For the therapeutic effect and fewer harm to foetus surgery and chemotherapy is that the better way to cure cancer. During surgery, doctors remove the tumour and few of the encircling healthy tissue. This poses little risk to the growing baby. Surgery also considered most safe treatment during all stages of pregnancy. Doctors also use chemotherapy to destroy certain kinds of cancer cells. But it is used during certain types of pregnancies. Administration of chemotherapy cannot be delayed until the top of pregnancy because the potential impact on maternal survival. The chemotherapy should generally be dosed according to the bodyweight of the pregnant women and dose are going to be adjusted consistent with to change in weight during treatment. The treatment should be preferred weekly and adverse effects are closely monitored. Physiological changes must be considered when prescribing the pregnancies. Additionally, most of the antineoplastic drug crosses the placenta thus adversely affect the placenta thus adversely affecting the fetus. Conversely, chemotherapy should be avoided during the primary embryonic and organogenesis periods as it might lead to fetal death and major malformations.

KEYWORDS: Cancer, pregnancy, chemotherapy, antineoplastic drug, malformations.

2. Introduction:

A rare occurrence of cancer and pregnancy and is estimated to account for only 1-2 cases per 1000 pregnancies. But Nowadays numbers have increased in recent years because of the increase in maternal age of 1st pregnancy. Possibility of transmission of malignancy from mother to child, to care about the optimal treatment to mother, and less harm to the foetus. It depends upon the period of disease treatment, the impact of treatment on pregnancy and other factor is the gestational period of pregnancy. Sometime, certain symptoms of cancer may be similar to pregnancy symptoms which can delay diagnosis. The common symptoms of both pregnancy and certain cancer include Bloating, headache, nausea, vomiting, breast changes, rectal bleeding. For the treatment of pregnancy, surgery is or chemotherapy is the better option to remove or reduce the tumour.

3.General Consideration:

In general, systemic therapy for cancer in pregnancy must be individualized and may be different if the patient is diagnosed during the first versus the second or third trimesters. Chemotherapy during the first trimester may cause more severe fetal effects, and in cases where a malignancy that requires chemotherapy is diagnosed during the first trimester, termination of pregnancy is a consideration.

For women who do not request pregnancy termination, the choice of drugs must take into account the fetus and may direct therapy to non-standard regimens. For malignancies diagnosed in the second trimester, consideration for the fetus concerning drug effects should be given, but in case of maternal cancer that responds to chemotherapy, it is unwise to delay treatment until after delivery. Termination of pregnancy is also a possibility, but the effect of the medications on the fetus will potentially be less than in the first trimester.

The likely adverse effects on the fetus have prompted practitioners to consider delaying chemotherapy until the postpartum period for cancers diagnosed in the third trimester. Although it is not prudent to put off definitive treatment for more than a few weeks, it may be possible to effect early delivery and proceed with chemotherapy in the postpartum period.[1,2]

i)Fetal Development and Potential Teratogenesis with exposure to Chemotherapy:

Chemotherapy drugs have different mechanisms of action, but most induce cell death by damaging DNA or RNA, or by inhibiting certain enzymes or proteins important for cell metabolism. Chemotherapeutic agents primarily affect rapidly dividing cells of the body, including both normal cells and tumour cells. Because of their high mitotic rate, cells of the developing foetus are very sensitive to chemotherapy and thus exposure to chemotherapy drugs may result in foetal death, malformations, or mental/physical retardations. Most common adverse effects in children exposed to intrauterine chemotherapy include growth retardation as well as head and limb anomalies.

Timing of exposure to a chemotherapeutic agent is the most important factor affecting the potential adverse effects on the foetus when using antitumoural drugs during pregnancy. Other factors including the type of chemotherapy drug, placental function, and maternal and foetal genetic and physiological status also play role in the occurrence of potential adverse effects. Chemotherapy is given during the first trimester of pregnancy result in the greatest chance of foetal death or malformation.

Women who had chemotherapy during the first trimester, exposure to chemotherapy early in pregnancy has been associated with increased risk of birth defects above the background risk. The chance for birth defects to happen is greatest when the fetus is exposed to chemotherapy during the first trimester of pregnancy. This is because the first trimester is when much of the baby's body is developing and cells are growing quickly. Exposure to chemotherapeutic drugs during the first trimester may also increase the chance for miscarriage and fetal deaths. If possible, chemotherapy should be avoided during the first trimester of pregnancy.

The chance of birth defects is less when chemotherapy is given in the second or third trimester. Most organ system development is completed by the beginning of the second trimester. However, the brain and the reproductive system may still be sensitive to some medications after the first trimester. Exposure to chemotherapeutic drugs in the second and third trimester has been associated with a greater chance for premature delivery (delivery before 37 weeks of

pregnancy), a higher rate of stillbirth, low birth weight, and a temporary reduction in some of the baby's blood cells (low blood counts).

ii) If a man has had chemotherapy, could it affect his fertility (ability to get a partner pregnant) or increase the chance of birth defects?

A man's ability to make sperm is often affected by cancer treatment. Sperm production may return to normal after chemotherapy, but it is not guaranteed. Also, damage to the structure of the chromosomes in sperm may happen. It is believed that most of the damage is not permanent, but some studies have found higher levels of abnormal sperm for years after the end of chemotherapy. Men who need cancer treatments may wish to consider sperm banking (freezing and storing) before treatment.[3,4]

4. Drugs use in chemotherapy:

1) Alkylating Agent:

Alkylating agent produces highly reactive carbonium ion intermediates or related transition complex which transfer alkyl group to cellular macromolecules by covalent bonds.

a) Cyclophosphamide:

commonly uses in ovarian cancer, breast cancer, lymphatic leukaemia Wilm's tumour. The mechanism of action of Cyclophosphamide is activated by liver cytochrome P450 to produce cytotoxic metabolites phosphoramidate mustard and acrolein. This agent cross-link with carboxyl, hydroxyl, amino, sulfhydryl and phosphate groups of biomacromolecules results from abnormal base pairing scission of DNA strand. A Cyclophosphamide is an alkylating agent with the most powerful immunosuppressive effects, widely used in the treatment of neoplasms and autoimmune diseases. For the lupus nephritis in pregnant women, cyclophosphamide is the first-line therapy. When cyclophosphamide administered an hour before a cesarean section, cyclophosphamide transfer the placenta and it can be detected in the amniotic fluid approximately 25% in concentration has been observed. If cyclophosphamide administered during the first trimester increases the rate of congenital malformations. The several reports have shown that the use of cyclophosphamide with anthracyclines in combination therapy, it can be relatively safe from the second trimester onward. Intravenous cyclophosphamide administered for severing exacerbation of systemic lupus erythematosus to the patient in the first trimester of pregnancy. Her neonates born with multiple anomalies, including absent thumbs, a birth defect of cyclophosphamide and indicate that judgement is required before its use in the first trimester.[5-12]

b) Busulfan:

Busulfan is commonly used chronic myelogenous leukaemia. Busulfan is the bifunctional alkylating agent interact with the thiol groups and nucleic acid to form DNA-DNA and DNA-protein cross-links. Cross-linking of DNA is results in inhibition of DNA synthesis and function. Busulfan is active in all phases the cell cycle. The drug is administered by either orally or intravenously. It is rapidly distributed in Plasma with broad tissue distribution, crosses the blood-brain barrier and placental barrier. If busulfan is administered to women in first trimester malformations including liver and spleen abnormalities, absent kidney and ureter. Cleft palate, Pyloric stenosis, microphthalmia.[13,14]

c)Melphalan:

Melphalan has been used to treat breast cancer, multiple myeloma, ovarian cancer. It is an analogue of nitrogen mustard. The main mode of action of melphalan is to form an interstrand and intra-strand cross-link with DNA, resulting in inhibition of DNA synthesis and function. Cell cycle non-specific as it acts in all stages of the cell cycle. The drug is administered orally as well as intravenously. It is distributed in amniotic fluid. The maternal toxicity of melphalan are as follows: ovarian failure, amenorrhea, hypersensitivity reaction.[15]

d)Thiotepa:

Thiotepa is helpful in the treatment of ovarian cancer, breast cancer, Hodgkin's and non-Hodgkin's lymphoma, treatment of superficial tumours of the bladder. Thiotepa is an ethylenimine analogue chemically related to nitrogen mustard which alkylates the N-7 position of guanine and inhibits the DNA, RNA and protein synthesis. It is primarily administered by the iv route. Widely distributed throughout the body. Thiotepa is used during the second and third trimester without apparent harm in a first pregnancy. In the pre-clinical trial, when rats were administered by the high dose of thiotepa many of the fetuses died in utero. Multiple malformations are common in surviving pups.[16,17]

e)Chlorambucil:

Chlorambucil is indicated for the treatment of chronic lymphocytic leukaemia and low grade, non-Hodgkin's lymphoma. It functions as a bifunctional alkylating agent. It is an analogue of nitrogen mustard that forms cross-links with DNA resulting in inhibition of DNA synthesis and function. Cell-cycle is non-specific. It is active in all phases of the cell cycle. The drug is given orally. After chlorambucil uses normal pregnancies as well as pregnancies complicated by fetus malformations. Other potential effects on a fetus are unilateral agenesis of left kidney and ureter in male foetuses following first-trimester exposure as well as cardiac defects.[18]

2]Vinca alkaloids:

They are also known as the aneuploidy inducer and are used in the treatment of leukaemia, lymphoma, breast cancer, testicular, bladder cancer, soft tissue sarcoma.

Vinblastine belongs to class of chemotherapy drug called alkaloid. Plant alkaloid are made from periwinkle plant. It inhibits cell division by interfering with the mitotic spindle. There are quite 15 case reports concerning the utilization of vinblastine during the first trimester, mostly in combination with other cytostatic drugs. In most of the cases, the pregnancy was normal. But some of the reports show children with malformations such as a child with hydrocephalus after intrauterine exposure to vinblastine alone in week 3, treatment with vinblastine until week 6 and spontaneous miscarriage shortly after injection of vinblastine in week 6.

Vincristine has been used to treat acute lymphoblastic leukaemia, Hodgkin's and non-Hodgkin's lymphoma, multiple myeloma, rhabdomyosarcoma, thyroid cancer, brain tumours, choriocarcinoma.

Vincristine is a vinca alkaloid derived from the periwinkle plant *Catharanthus roseus*. The main mechanism of vincristine is inhibition of tubulin polymerization and disrupts mitosis; hence drug is active during the M-phase of cell cycle. It is given intravenously, and distributed throughout the body. Various reports of vincristine use in pregnancy and associated with fetal anomalies have appeared. There are quite 20 case reports regarding apparently normal children following vincristine therapy during the first trimester. However, there are also reports of an

aborted fetus with renal aplasia after combination therapy. A child with a congenital defect after vincristine treatment until week 6; a receiving combination therapy for Hodgkin's disease during the first trimester whose hydrocephalic child died four hours after birth. Some reports show that normal pregnancies after exposure during the second and third trimesters.

Vinorelbine may be indicated to treat non-small cells lungs cancer, breast cancer, ovarian cancer, and Hodgkin's lymphoma. It is a semi-synthetic form of vinblastine with similar actions, it is given intravenously, distributed throughout the body and is 80% bound. Pregnancy with vinorelbine and trastuzumab in the third trimester was complicated by oligohydramnios.[19,20]

3]Taxanes:

a)Paclitaxel:

Paclitaxel is used in the treatment for breast cancer, lungs cancer, head and neck cancer, prostate cancer, ovarian cancer, bladder cancer. Taxanes are a class of diterpenes. They were originally identified from plants of genus *Taxus*(yews), and feature a taxadienen core. Paclitaxel is obtained from, *Taxus brevifolia* and docetaxel (Taxotere) are widely use as chemotherapy agents. The mechanism of this agent is binding to microtubule and enhancing polymerization. Mitosis is inhibited by M-phase of the cell cycle. It is given by intravenously and distributed throughout the body but poor blood-brain barrier penetration. Rare cases of anaphylaxis have been reported. The most common adverse event was oligohydramnios and/or hydramnios (16.6%), mainly attributed to trastuzumab (coadministration in 75% of cases with oligohydramnios and/or hydramnios).[21,22]

b)Docetaxel:

It has a higher tissue affinity than paclitaxel. In addition, CYP3A4, one of the enzymes that metabolize taxanes, is not expressed in fetal livers. For this reason, embryotoxicity and fetotoxicity are enhanced, suggesting an increased likelihood of intrauterine fetal death (IUFD) and decreased body weight. However, no increase in fetal and maternal complications during pregnancy with use of taxanes, when compared with conventional chemotherapy during cohort study conducted in clinical practice.[23]

4]Antimetabolites:

a)Methotrexate:

Methotrexate is also indicated for haematological and breast cancer treatment and its oral formulation is widely used as an anti-rheumatoid arthritis drug. Methotrexate is classic folic acid antagonist, and its action is specific for the S- phase of the cell cycle. The drug enters the cell through folate transport system and inhibits the enzyme dihydrofolate reductase, thus depleting the level of reduced folates necessary for critical cell function. Methotrexate also inhibits de novo thymidylate and purine synthesis.it is distributed throughout the body including amniotic fluid spaces such as the amniotic fluid. The drug is administered by the intravenous, intramuscular or oral routes. In the first trimester, clearly associated with teratogenicity malformations include Absence of frontal bone, absence of sutures, hypertelorism, hypoplasia, the mandible of the mandible, a depressed or widened nasal bridge, heart defect. The attack rate is relatively high; nearly one-third of exposed fetuses demonstrate malformations.[24]

b)5-Fluorouracil:

5-Fluorouracil is used in the treatment of ovarian cancer, breast cancer, skin cancer, head and neck cancer, hepatoma and gastrointestinal cancer. This agent is pyrimidine analogue specific for S-phase for the cell cycle. metabolic forms are incorporated into DNA and RNA to disrupt cell function. In one report, first-trimester treatment was associated with multiple anomalies like hypoplasia of thoracic and abdominal organ such as lungs, aorta, oesophagus, duodenum and ureters. radial dysplasia also is seen.[25,26]

5]Antibiotics:**a)Doxorubicin:**

Doxorubicin is the most frequent use of anthracycline antibiotics. It is indicated for ovarian cancer, lungs cancer, soft tissue sarcoma, hepatoma, Wilm's cancer, bladder cancer, gastric cancer, and lymphoblastic leukaemia. Doxorubicin is isolated from *Streptomyces* species that intercalate into DNA, results in inhibiting DNA synthesis. The drug also inhibits the transcription, by inhibiting DNA dependent RNA polymerase. Doxorubicin accumulates in the placenta, and the parent drugs, as well as its metabolites, have been detected in fetal tissues. Adverse pregnancy outcomes, including preeclampsia at 28 weeks gestation, intrauterine growth restriction, and fetal demis have been reported when doxorubicin was administered during mid- or late pregnancy. However, doxorubicin appears to have a relatively better safety profile for the post-first trimester foetus when compared with other anthracyclines. The lack of optimization of doxorubicin dosage regimen in pregnancy potentially impacts the efficacy and safety of these patients.[27-29]

b)Bleomycin:

Bleomycin is indicated for germ cell tumours, head and neck cancer, squamous cell carcinomas of the skin, cervix, and vulva. Bleomycin is a small peptide antibiotic. The main mechanism is binds iron to create activated oxygen-free radicals causing breaks in DNA. It is administered by intravenously. The major teratogenic effect is pneumonitis, which is dose-limiting. Chromosomal aberrations in human bone marrow cell have been reported.[30-32]

6]Hormonal Agents:

Hormones are the chemicals made by glands, such as ovaries and testicles. Hormone therapy as a cancer treatment may involve taking medicines that block the activity of the hormone or stop the body from making the hormone. Hormone therapy may involve surgically removing a gland that is making the hormones.

The most common side effect of hormone therapy is vaginal dryness, hot flashes, loss of bone density, loss of libido (sex drive), weight gain, mood swings, fatigue, nausea and vomiting. Many of the hormonal agents show side effects, for example,

a)Tamoxifen:

Tamoxifen is used in patients with breast cancer which demonstrates sensitivity toward premenopausal hormones. However, regarding the effects of tamoxifen during pregnancy, the available case reports involve recurrent breast cancer, and no obvious tumour-shrinking effect was observed due to tamoxifen. Besides, regarding safety, since a relationship with congenital abnormalities (including golden hair syndrome, ambiguous genitalia and Pierre Robin

syndrome) has been suggested, tamoxifen should never be used at any stage during pregnancy. If hormone therapy is required, it should be administered during the postpartum period.[34]

b)Anastrozole:

Anastrozole is another drug from hormone therapy, anastrozole is contraindicated in women who are pregnant or who become pregnant because it increased pregnancy loss or pregnancy failures, signs of delayed fetal development, significant incidences on infertility. Anastrozole may enter breast milk it is unclear what effect this may have on babies.[35]

c)Diethylstilboestrol :

Diethylstilboestrol is used in the treatment of breast cancer if it is given during pregnancy it shows recurrent miscarriage. The US FDA subsequently withdrew approval of DES as a treatment for pregnant women. DES also has the potential to cause a variety of significant adverse medical complications during the lifetimes of those exposed. DES has been linked to a variety of long-term adverse effects, such as the increased risk of vaginal clear-cell adenocarcinoma, vaginal adenosis, T-shaped uterus, uterine fibroids, cervical weakness, infertility, hypogonadism, intersex defects, depression. The US National Cancer Institute recommends women born to mothers who took DES to undergo special medical exams regularly to screen for complications as a result of the medication. individuals who were exposed to DES during their mother's pregnancies are commonly referred to as "DES daughters" and "DES sons". Since the discovery of the toxic effects of DES, it has largely been discontinued and is now mostly no longer marketed.[36]

d)Flutamide:

Flutamide is not indicated for use in females. Flutamide can cause harm to your unborn baby if given to a pregnant woman. It has a metabolite that can cause methemoglobinemia, haemolytic anaemia and cholestatic jaundice. Flutamide focuses on category D. It has been shown that the use of flutamide in pregnant women caused some babies to be born with problems. However, in some serious situations, the benefit of using this medication may be greater than the risk of harm to the baby. According to the manufacturer, this product is not indicated for use in women. There have been postmarketing reports of hospitalization and rarely death due to liver failure in patients taking flutamide. Evidence of hepatic injury included elevated serum transaminase levels, jaundice, hepatic encephalopathy and death related to acute hepatic failure. The hepatic injury was reversible after discontinuation of therapy in some patients. There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans. but potential benefits may warrant the use of the drug in pregnant women despite the potential risk.[37]

e)Goserelin:

Gosereline medication should not be taken during pregnancy as it may harm the unborn baby. In animal studies, pregnant animals were given this medication and had some babies born with problems. Administration during organogenesis resulted in increased preimplantation loss and increased resorptions. There is an increase in umbilical hernia in offspring and decreased foetus and pup survival. There are no controlled data in human pregnancy. It is not known whether goserelin passes into breast milk or if it could harm a nursing baby. Should not breastfeed while the implant is in place.

According to the data of hormonal agents, it is assumed that hormone therapy should not be given during pregnancy because it can affect the baby. It should be delayed until after the woman has given birth.[38]

Table-1: Chemotherapeutic agents and teratogenicity

Chemotherapeutic agent	Recommendations for administration during pregnancy	Teratogenic effect
Methotrexate	Contraindicated	Absence of frontal bone, absence of sutures, hypertelorism, hypoplasia, the mandible of the mandible, a depressed or widened nasal bridge, heart defect.
Alkylating agent (cyclophosphamide)	Applicable in distinct cases	Cleft pallet
Anthracyclines (doxorubicine, epirubicine, idarubicine)	Considered in 2 nd and 3 rd trimester	Cardiotoxicity
Taxane	Not recommended due to limited data	Intrauterian fetal death
5-Fluorouracil	Considered in 2 nd and 3 rd trimester	hypoplasia of thoracic and abdominal organ such as lungs, aorta, oesophagus, duodenum and ureters. radial dysplasia also is seen.
Bleomycine	Not recommended due to limited data	Pneumonitis
Vinca alkaloids	Not recommended due to limited data	A child with a congenital defect

<p>Monoclonal antibodies</p> <ol style="list-style-type: none"> 1. Bevacizumab 2. Trastuzumab 	<p>Contraindicated</p> <p>Not recommended due to limited data.</p> <p>Applicable if strictly indicated after informed consent.</p>	<p>Can cause cardiotoxicity</p>
<p>Tyrosine kinase inhibitor</p> <ol style="list-style-type: none"> 1. Sunitinib 2. Sorafenib 3. Anti-endocrine therapy 	<p>Contraindicated</p> <p>Contraindicated</p> <p>contraindicated</p>	<p>Embryotoxicity, fetotoxicity in animals.</p> <p>Fetal skeletal malformations of the ribs and vertebrae.</p>

5. Radiotherapy during pregnancy:

Radiotherapy should be avoided during pregnancy due to the teratogenic effect on the foetus. Generally, pregnant women with cancer should be avoided or delay the radiotherapy until after delivery.^{1,2,3} Radiotherapy may harm foetus like mental retardation, growth restriction, organ malformations, intrauterine growth restriction, carcinogenesis⁴. Radiation dose with >100-200mGy; however, a lower dose may cause the development of cancer or leukaemia in childhood and sterility.^{1,4} Such radiation therapy requires meticulous planning and shielding, expertise, involve some risk of the fatal defect and carries the risk of litigation. Most experts do not advice for radiation therapy during pregnancy.[39-42]

Table-2: Effect of radiation on pregnant women

Gestational age	Effect	Threshold dose
0-2weeks	Death or no consequence	50-100 mGy
2-8weeks ⁹	Congenital anomalies Growth retardation Childhood leukemia	200 mGy 200-250 mGy
8-15weeks	Severe mental retardation Intellectual deficit microcephaly	60-310 mGy 200 mGy 200 mGy
16-25week	Severe mental retardation	250-280 mGy

6. Maternal/ fetal outcome:

Pregnancy does not seem to modify the biology and prognosis of cancer, neither do subsequent pregnancies increase the risk for relapse. Still following cancer treatment a woman is advised to wait for anything from 6 months to 2-5 years before embarking on childbearing. Placental metastases are extremely rare. when metastases are extremely rare, when seen melanoma, breast cancer and leukaemia. chemotherapy during embryogenesis increased risks of spontaneous abortions and major birth defects and stillbirth, fetal growth restriction, premature birth, and maternal and fetal myelosuppression.

7. Things About Cancer During Pregnancy :

1) How is cancer detected in pregnant women?

A cancer diagnosis during pregnancy is a rare occurrence. It is estimated that this coexistence only affects 1 in every 1000 pregnant women. cancer is especially difficult to detect in pregnant women. Pregnant women experience many changes in their body as the fetus grows. Some common changes include bloating, headaches, nausea, vomiting, fatigue, breast changes, and rectal bleeding. While considered normal in pregnancy, these are also common symptoms of cancer. Because of this overlap, cancer diagnoses are typically delayed in pregnant women.

2) What kind of cancers are common among pregnant women?

The most common cancer amongst pregnant women is breast cancer, affecting approximately 1 in 3000 pregnant women. Pregnant women may also be affected by cervical cancer, thyroid cancer, Hodgkin lymphoma, non-Hodgkin lymphoma, melanoma or gestational trophoblastic tumour. Pregnant women may be diagnosed with nearly any type of cancer, though these cancers are more likely to affect younger women.

3) Are diagnostic tests and treatment safe while pregnant?

Many of commonly used diagnostic tests are safe for both the women and the baby. this includes X-Rays, magnetic resonance imaging (MRI), computed tomography (CT) scans, ultrasounds and biopsies. X-rays and scans, however, should be used cautiously due to the radiation. The radiation produced from X-Rays has been proven to be too low to cause harm to a fetus. Both surgery and chemotherapy can be safe for the woman and the fetus. Depending upon the drug, the health team recommend waiting until after the first trimester (when the baby's organs developed) or waiting until after the birth to start chemotherapy.

4) How will cancer affect pregnancy?

Cancer rarely affects the baby during pregnancy. If administered in the first trimester, chemotherapy may cause birth defects or pregnancy loss. Administering chemotherapy after the first trimester has far less severe risk, the most important being possible preterm birth and the possibility of babies being small for gestational age. While these are important risks to be aware of, they are not necessarily common. Once the baby is born, the mother can continue with treatment. if receiving chemotherapy, however, she should not breastfeed as the drugs can transfer through breastmilk.[43]

8. Conclusion:

Cancer during pregnancy is rare, it can and does happen to some women. Often a pregnant woman with cancer has the same outlook as a woman with cancer who isn't pregnant. Chemotherapy involves using a toxic substance to kill cancer in the body. The care provider has to manage two lives: the life of a woman suffering from a disease that if left untreated is likely to progress, and the life of a fetus exposed to damage from maternal chemotherapies administered. Chemotherapy and other anticancer drugs can harm the fetus, cause birth defects or lead to miscarriage, especially if they are used during the first trimester of pregnancy. The risk for damage is more likely during the first three months of pregnancy, that is the first trimester because during this baby's organs and body structure are developing. consulting with the doctor about the best way to treat cancer during pregnancy. Many women go on to recover from cancer and have healthy babies.

9. References:

1. Esposito S, Tenconi R, Preti V, Groppali E, Principi N. Chemotherapy against cancer during pregnancy. A systemic review on neonatal outcome, *Medicine*. 2016;95(38):e4899.
2. Salani R, Billingsley C, Crafton S. Cancer and pregnancy: an overview for obstetricians and gynecologists. *American Journal of Obstetrics and Gynecology*. 2014;211(1):7-14.
3. Leslie K, Koil C, Rayburn W. Chemotherapeutic Drugs in Pregnancy. *Obstetrics and Gynecology Clinics of North America*. 2005;32(4):627-640.
4. Cancer in Pregnancy: Types, Treatment, Risks, and Outlook [Internet]. Healthline. 2020 [cited 8 August 2020]. Available from: <https://www.healthline.com/health/cancer-in-pregnancy>
5. Lannes G, Elias F, Cunha B, Jesus N, Klumb E, Albuquerque E et al. Successful pregnancy after cyclophosphamide therapy for lupus nephritis. *Archives of Gynecology and Obstetrics*. 2011;283(S1):61-65.
6. Miyamoto S, Yamada M, Kasai Y, Miyauchi A, Andoh K. Anticancer drugs during pregnancy. *Japanese Journal of Clinical Oncology*. 2016;46(9):795-804.
7. D'Incalci M, Sessa C, Colombo N, de Palo G, Semprini AE, Pardi G. Transplacental passage of cyclophosphamide. *Cancer Treatment Reports*. 1982;66(8):1681-1682.
8. Avilés A, Díaz-Maqueo J, Talavera A, Guzmán R, García E. Growth and development of children of mothers treated with chemotherapy during pregnancy: Current status of 43 children. *American Journal of Hematology*. 1991;36(4):243-248.
9. Pizzuto J, Aviles A, Noriega L, Niz J, Morales M, Romero F. Treatment of acute leukemia during pregnancy: presentation of nine cases. *Cancer Treat Rep*. 1980;64(4-5):679-683.
10. Amant F, Deckers S, Van Calsteren K, Loibl S, Halaska M, Brepoels L et al. Breast cancer in pregnancy: Recommendations of an international consensus meeting. *European Journal of Cancer*. 2010;46(18):3158-3168.
11. Cardoso F, Loibl S, Paganì O, Graziottin A, Panizza P, Martincich L et al. The European Society of Breast Cancer Specialists recommendations for the management of young women with breast cancer. *European Journal of Cancer*. 2012;48(18):3355-3377.

12. Kirshon B, Wasserstrum N, Willis R, Herman GE, McCabe ER. Teratogenic effects of first-trimester cyclophosphamide therapy. *Obstet Gynecol.* 1988;72(3 Pt 2):462-464.
13. Lee RA, Johnson CE, Hanlon DG. Leukemia during pregnancy. *Am J Obstet Gynecol* 1962;84: 455 – 8.
14. Diamond I, Anderson MM, Mc Creadie SR. Transplacental transmission of busulfan (myleran) in a mother with leukemia. Production of fetal malformation and cytomegaly. *Pediatrics* 1960; 25:85 – 90.
15. Rose D, Davis T. OVARIAN FUNCTION IN PATIENTS RECEIVING ADJUVANT CHEMOTHERAPY FOR BREAST CANCER. *The Lancet.* 1977;309(8023):1174-1176.
16. Dobbing J. Pregnancy and leukaemia. *Lancet (London, England).* 1977 May;1(8022):1155. DOI: 10.1016/s0140-6736(77)92416-3.
17. MURPHY ML, DEL MORO A, LACON C. The comparative effects of five polyfunctional alkylating agents on the rat fetus, with additional notes on the chick embryo. *Annals of the New York Academy of Sciences.* 1958 Apr;68(3):762-81; discussion 781-2. DOI: 10.1111/j.1749-6632.1958.tb42639.x.
18. Shotton D, Monie Iw. Possible Teratogenic Effect Of Chlorambucil On A Human Fetus. *JAMA.* 1963;186:74-75. doi:10.1001/jama.1963.63710010031022c
19. Corinna Weber-Schöndorfer, Christof Schaefer, in *Drugs During Pregnancy and Lactation, vinca alkaloids and structural analogs (Second Edition)*, 2007
20. Jorge J. Castillo, Tina Rizack, in *Abeloff's Clinical Oncology, Special issue in pregnancy*, science direct (Fifth Edition), 2014, 914-925
21. Zagouri, F., Sargentanis, T., Chrysikos, D., Dimitrakakis, C., Tsigginou, A., Zografos, C., Dimopoulos, M. and Papadimitriou, C., 2013. Taxanes for Breast Cancer During Pregnancy: A Systematic Review. *Clinical Breast Cancer*, 13(1), pp.16-23.
22. Miyamoto, S., Yamada, M., Kasai, Y., Miyauchi, A. and Andoh, K., 2016. Anticancer drugs during pregnancy. *Japanese Journal of Clinical Oncology*, 46(9), pp.795-804.
23. Cardonick E, Bhat A, Gilmandyar D, Somer R. Maternal and fetal outcomes of taxane chemotherapy in breast and ovarian cancer during pregnancy: case series and review of the literature. *Ann Oncol.* 2012;23(12):3016-3023. doi:10.1093/annonc/mds170
24. Krishnansu S. Tewari M.D., in *Clinical Gynecologic Oncology (Seventh Edition)*, 2007
25. Peccatori F, Azim H Jr, Orecchia R, et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2013;24 Suppl 6:vi160-vi170. doi:10.1093/annonc/mdt199
26. Dreicer R, Love RR. High total dose 5-fluorouracil treatment during pregnancy. *Wis Med J.* 1991;90(10):582-583.
27. d'Incalci M, Broggin M, Buscaglia M, Pardi G. Transplacental passage of doxorubicin. *Lancet.* 1983;1(8314-5):75. doi:10.1016/s0140-6736(83)91614-8
28. Karp GI, von Oeyen P, Valone F, et al. Doxorubicin in pregnancy: possible transplacental passage. *Cancer Treat Rep.* 1983;67(9):773-777.
29. García L, Valcárcel M, Santiago-Borrero PJ. Chemotherapy during pregnancy and its effects on the fetus-- neonatal myelosuppression: two case reports. *J Perinatol.* 1999;19(3):230-233. doi:10.1038/sj.jp.7200138

30. Cardonick E, Iacobucci A. Use of chemotherapy during human pregnancy. *Lancet Oncol.* 2004;5(5):283-291. doi:10.1016/S1470-2045(04)01466-4
31. Bornstein RS, Hungerford DA, Haller G, Engstrom PF, Yarbrow JW. Cytogenetic effects of bleomycin therapy in man. *Cancer Res.* 1971;31(12):2004-2007
32. de Vries EG, van der Zee AG, Uges DR, Sleijfer DT. Excretion of platinum into breast milk [published correction appears in *Lancet* 1989 Apr 8;1(8641):798]. *Lancet.* 1989;1(8636):497. doi:10.1016/s0140-6736(89)91396-2
33. Ortega J. Multiple agent chemotherapy including bleomycin of non-Hodgkin's lymphoma during pregnancy. *Cancer.* 1977;40(6):2829-2835. doi:10.1002/1097-0142(197712)40:6<2829::aid-cnrcr2820400613.
34. Braems, G., Denys, H., De Wever, O., Cocquyt, V. and Van den Broecke, R., 2011. Use of Tamoxifen Before and During Pregnancy. *The Oncologist*, 16(11), pp.1547-1551.
35. Teresa Brucker, P., Anyssa Garza, P., Katrina Korn, P. and Cara Clayton, P., 2020. *Anastrozole Rxwiki*. [online] rxwiki. Available at: <<https://www.rxwiki.com/anastrozole>> [Accessed 8 September 2020].
36. Hilakivi-Clarke L. Maternal exposure to diethylstilbestrol during pregnancy and increased breast cancer risk in daughters. *Breast Cancer Research.* 2014;16(2).
37. Giorgetti A, Centola C, Giorgetti R. Fentanyl novel derivative-related deaths. *Human Psychopharmacology: Clinical and Experimental.* 2017;32(3):e2605.
38. Moore HC, Unger JM, Phillips KA, et al. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. *N Engl J Med.* 2015;372(10):923-932. doi:10.1056/NEJMoa1413204
39. Kal HB, Struikmans H. Radiotherapy during pregnancy: fact and fiction. *Lancet Oncol.* 2005;6(5):328-333. doi:10.1016/S1470-2045(05)70169-8
40. Peccatori FA, Azim HA Jr, Orecchia R, et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2013;24 Suppl 6:vi160-vi170. doi:10.1093/annonc/mdt199
41. Amant F, Deckers S, Van Calsteren K, et al. Breast cancer in pregnancy: recommendations of an international consensus meeting. *Eur J Cancer.* 2010;46(18):3158-3168. doi: 10.1016/j.ejca.2010.09.010
42. Fenig E, Mishaeli M, Kalish Y, Lishner M. Pregnancy and radiation. *Cancer Treat Rev.* 2001;27(1):1-7. doi:10.1053/ctrv.2000.0193 Hepner A, Negrini D, Hase EA, et al. Cancer During Pregnancy: The Oncologist Overview. *World J Oncol.* 2019;10(1):28-34. doi:10.14740/wjon1177
43. Zemlickis D, Lishner M, Degendorfer P, Panzarella T, Sutcliffe SB, Koren G. Fetal outcome after in utero exposure to cancer chemotherapy. *Arch Intern Med.* 1992;152(3):573-576.