DHR Proceedings

Special Edition: Junior Clinical Research (2023), Vol. 3 No. S2
https://doi.org/10.47488/dhrp.v3iS2.80

COMMENTARY

Factors/Maternal Behaviors That Affect Fetal Development

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Received: June 16, 2023
Accepted for publication: October 25, 2023
Published: November 16, 2023

Introduction

Since the dawn of time, birth defects have always been a major issue. Birth defects can be described as a complication that occurs during fetal development in the mother's body[1]. According to the Centers for Disease Control and Prevention (CDC), one in thirty-three neonates are born with a birth defect.[2] These congenital anomalies can eventually advance to emergency situations as their life progresses.[2] Some of the factors that may affect birth outcomes are viruses, the influence of the environment, genetics (interbreeding), and complications during pregnancy/labor. Other contributing factors to fetal development include behaviors such as drugs, alcohol, smoking, and diet. Since 20% of newborn fatalities are due to birth defects, it is vital for mothers to be aware of these factors and behaviors.[3] Therefore, our goal is to provide information to implement preventative measures for outcomes of prenatal malformations.

Alcohol

Consuming alcohol during fetal development causes a number of alcohol-induced defects known as fetal alcohol spectrum disorder (FASD).[4] Alcohol can affect the fetus in its early stages even if the woman is not aware she is pregnant. It has been reported that 20-30% of women drink at some point during the first trimester. Drinking may cause stunted growth of the brain resulting in educational, behavioral, medical, and social-related problems.

Types of educational issues may include but are not limited to working memory, problem-solving, and impairments in reading, spelling, and math skills.[5] A child with FASD may experience aggressive behavior, extreme mood changes, hyperactivity, and impulsiveness.[6] Some medical issues include narrow eye openings, a smooth area between the lip and nose, and a thin upper lip.[7] Social-related problems include unresponsiveness to social cues and the inability to keep/make friends.[8]

Drugs & Smoking

North America is living through a rapid increase in opioids and cannabis consumption, including prescription and non-prescription drugs.[9] Since 1999, the incidence of NAS has increased by 300%.[9] Pregnant women are not immune to disorders resulting from drugs. It is estimated that 10% of births each year are affected negatively by illicit drug use.[9] During the nine-month pregnancy process, drug use may not only be addictive but can affect the mother and the fetus negatively. There are many types of medication that can be used in a positive manner, but the mothers using these medications can become reliant on them. Opioids are used to manage pain,

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which can lead to addictive behaviors from the mother, affecting the fetus, specifically causing the newborn also to be dependent on the specific drug used. Other consequences include labor miscarriages, premature delivery, cognitive developmental problems, abnormal brain structure, and function, as well as fetal stress.[10]

The prevalence of drug use in pregnancy is not accurately represented due to the small amount of well-validated tests.[9] There are no specific guidelines for drug screening during pregnancy, so the number of affected births is unknown.[9] Cooperation from the mothers is also very limited. Only 5% of women admit to the doctor that they were taking drugs during pregnancy.[9] This can lead to invalidated results and inaccurate diagnoses. Although the amount is small, tests are still available to see if the mother is misusing drugs. Various tissues are tested for drug use, including maternal blood, urine, umbilical cord tissue, and hair.[9] Other tests include simple spectrophotometry or sophisticated analytical HPLC.[9] Certain US states, including Tennessee, Alabama, and South Carolina, have charged the women with child abuse if they are found addicted to drugs, and multiple women have been arrested if their drug screens are positive.[9]

Women are at the highest risk of developing a substance use disorder during their developmental age (18-24).[11] In a national survey, taken in 2012 in the United States, results show that 5.9% of women use illicit drugs, and 15.9% smoke cigarettes, resulting in 380,000 offspring being exposed to illicit drugs and over one million being exposed to tobacco, though 54% of women who smoke quit before pregnancy.[11] The most commonly used substances during pregnancy are tobacco and nicotine, which if used, expose the newborn to the risk of health problems, learning disabilities, and brain developmental abnormalities. Studies of the ACOG clinical research show that children born to smoker women during or before pregnancy are at risk of bone fractures, asthma, child respiratory infections, as well as hearing loss.

Drug consumption can imply a young woman with health complications. Drug abuse during pregnancy may cause many problems such as miscarriage, preterm labor, birth defects, stillbirth, withdrawal symptoms for the mother and baby after birth, a high risk of sudden infant death syndrome (SIDS), poor fetal growth rate, and cognitive and behavioral problems.[12] Also, women that inject drugs during birth are at a higher risk of contracting HIV, which is commonly passed down to their babies.[12]

Non-prescription drugs are not the only substances that present risks to the woman's health. Prescription drugs, specifically prescribed opioids, are also at risk to women, with many reports of women getting addicted to prescription drugs and painkillers.[12] These drugs can also cause serious withdrawal symptoms in newborn babies.[12] This is commonly known as neonatal abstinence syndrome (NAS).

Neonatal Abstinence Syndrome (NAS) is a mass of symptoms that indicate a newborn is going through withdrawal symptoms because of exposure to opioids during the mother's pregnancy.[13] The most common drugs associated with NAS are heroin, codeine, fentanyl, oxycodone, and methadone.[13] Some symptoms of neonatal abstinence syndrome are vomiting, fever, sleep problems, seizures, rapid breathing, and many more.[13] NAS is treatable. Many doctors recommend taking medicine that helps with withdrawal symptoms, injecting fluids through the vein of the newborn so it does not get dehydrated, and being fed higher-calorie baby formula.[14]

Although many states have introduced counseling and pregnancy-specific materials to help mothers that are dependent on a certain drug or smoke consistently, some women continue to use tobacco products and drugs.[15] Many surveys show that it is also recommended that clinicians individualize care by providing psychosocial, behavioral, and pharmacotherapy interventions to mothers that are either addicted to drugs or that smoke.[15]. Many physicians and doctors are working on significantly decreasing the amount of drug use in North America, not just in pregnant women, but in the whole population.

Diet

Women have specific nutritional requirements during pregnancy and breastfeeding when the nutritional vulnerability is most common.[16] Nutrients include carbohydrates (sugars), lipids (fats), proteins, specific vitamins, minerals, and water.[17] Poor diets lacking nutrients like iodine, zinc, folate, and calcium increase the risk of anemia, pre-eclampsia, and hemorrhage in mothers and can cause the child to be stillborn, and have a low birthweight - UNICEF estimates low birthweight affects about 20 million newborns each year - and can create many developmental problems.[16] There are many foods that should be avoided during pregnancy. These foods can cause certain birth defects in the fetus and can increase the risk of foodborne illnesses for the mother.

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Seafood can provide an amazing source of protein and omega-3 fatty acids for the mother. Protein and fatty acids can positively affect the newborn's brain and eye development. However, certain shellfish have high levels of mercury which can harm the newborn's nervous system.[18] The older and bigger the fish, the more mercury it is likely to contain.[18] The FDA encourages mothers to stay away from bigeye tuna, marlin, king mackerel, shark, and wordfish to avoid the risk of these problems. Any raw, contaminated, or undercooked seafood should also be avoided due to the risk of contamination.[18]

During pregnancy, mothers are at a higher risk of contracting bacterial food poisoning, and the reaction might be more severe than if the mother wasn't pregnant.[18] Undercooked meat, poultry, and eggs are foods that can carry bacteria that can affect the mother, and possibly the baby.[18]

Unpasteurized foods can lead to foodborne illnesses. Any low-fat products, such as low-fat milk or mozzarella, are healthy for the diet. Raw milk, also known as unpasteurized milk, can contain bacteria such as campylobacter, E. coli, listeria, or salmonella. Pregnant women are at higher risk of contracting these types of bacteria, and the reactions resulting from them will be more severe.[19] These bacteria are also very common on unwashed fruits and vegetables and raw sprouts of any kind.[18]

The effects of caffeine and herbal teas on newborns are not clear, but doctors suspect they are negative. Although caffeine can cross the placenta, the effects of it on newborns aren't clear, so doctors recommend avoiding excess caffeine, just to be safe.[17] There also is not much information on herbal teas and their effect on developing babies though doctors recommend that mother avoid these types of teas.[18] Despite this, there are specific herbal teas that encourage pregnant women to drink them.[18]

There is a mass amount of vitamins the baby needs to have a smooth development. For example, a significant lack of Vitamin B may cause birth defects and stillbirth. Calcium during pregnancy can significantly decrease the risk of contracting preeclampsia, a disease that causes a sudden increase in blood pressure.[17] Calcium also builds up the newborn's bones and teeth. A significant lack of calcium can cause the baby's bones to be brittle and can increase the risk of fractures and broken bones. Vitamin D helps the calcium in the body to build up the newborn's bones and teeth.[17]

A balanced diet is important for both the mother and the newborn. If one element or vitamin overweighs the others, many defects and problems can occur. A stabilized diet will provide the baby with optimal nutrition and condition for the developmental process to go smoothly and without any setbacks or problems.[18]

Viruses

The environment of the fetal development holds great significance in the development of the infant during pregnancy, more so when it includes viral infections in the mother's body which will inevitably affect the outcome of the pregnancy.[20] Pathogens that contribute to neurodevelopmental disorders include the rubella virus, herpes simplex virus, Influenza A virus, and CMV. Studies have shown that infections that present during a mother's pregnancy; sinusitis, pneumonia, pyelonephritis, or bacterial venereal disease, are linked to increasing the child's neurodevelopmental risk by 2 times. This can be very extremely dangerous for the infant as it will elevate the risk of ASD, which is a main portion of illnesses that are discovered.[21] The danger lies in the possible long-term effects such as congenital anomalies or in some cases, death. The World Health Organization (WHO) has stated that of the 5,000,000 neonatal deaths that occur worldwide per year, approximately 2,000,000 are directly the result of infection.[22]

Influence of Environment

During a woman's pregnancy, it is crucial that she is in a safe environment. Many small little things can affect the pregnancy, ultimately affecting the fetus's development as well, if the mother is exposed to certain things. Domestic violence for pregnant women between the ages of 18-60 negatively affects obstetric-related outcomes as well as mental health during the postnatal period.[23] Exposure to violence during the woman's pregnancy can lead to consequences such as hemorrhage, preterm rupture of membranes, recurrent miscarriages, premature placental abruption, and low birth weight.[23] Both the baby's growth and the postpartum period may be seriously harmed by this. During pregnancy, it's crucial that the woman is in a secure setting. If the mother is not in a safe environment and experiencing domestic violence it can lead to factors of stress, depression, or suicidal tendencies. Depression is the most common causing the mother to lose interest in daily activity, ultimately affecting the fetus as well.[24] One most seen types of depression during pregnancy

is perinatal depression. This can leave the mother in a depressed state, which eventually leads to future health issues. If left untreated it can pose maternal risks such as preeclampsia, placental abruption, cesarean delivery, preterm admission, and maternal postpartum readmission.[24] Long-term neurodevelopmental consequences in offspring can also be presented during pregnancy if perinatal depression is not treated right away.[24] Pregnancy nutrition is important because it provides the fetus with the nutrients it needs for maturation into a healthy child. The fetus would also be adversely affected if the mother was not getting adequate nourishment. One major part of pregnancy is that the fetus is totally dependent on the mother's vitamin status.[25] Vitamin D is critical for bone and calcium homeostasis as well as preventing neonatal hypocalcemia and pre-eclampsia.[25] Studies show that vitamin D deficiency is associated with postpartum depression which is why the status of vitamins is important in brain development, cognitive function, fetal bone growth, and neonatal lung maturation.[25] During stages of the woman's pregnancy, there can be complications along the way but it is crucial that she remains in a safe environment as it can show to have an effect on fetal development. During pregnancy, a variety of circumstances may arise, but the mother's decision to remain in a healthy environment is paramount for the mother and developing child.

Genetics: Age, Interbreeding

Birth defects are mainly caused by malformations in the genetic composition of a fetus and are usually shown during the early stages of pregnancy, usually by the end of the first trimester.[26] Some of these malformations are influenced by the mother's medical conditions, mutations in the genes, chromosomal abnormalities, single-gene defects, and dominant traits.[27] Chromosome abnormalities occur during the formation of reproductive cells or during early fetal development. These errors usually occur during the cell division process (meiosis and mitosis) when there are problems with the duplication and deletion of chromosomes. Aside from numerical abnormalities in chromosomes, there are also structural changes in chromosomes that can lead to birth defects.[27]

Chromosomes come in pairs, so the number becomes imbalanced when there is a missing chromosome (monosomy) or when there is an extra chromosome (trisomy).[28] Fetuses that suffer from trisomy often lead to miscarriage, but those who survive are diagnosed with moderate to severe birth defects.[28] This is commonly seen in Down Syndrome patients who have an extra copy of chromosome 21, also known as trisomy 21. Studies have shown that this abnormality usually originates from the mother due to age.[29] Other medical conditions that are caused by chromosomal deletion include heart defects, palatal abnormalities, learning difficulties, facial deformities, and psychiatric disorders in older patients like schizophrenia and bipolar disorder.[30]

Balanced translocations do not alter the number of chromosomes, but they alter the structure of a chromosome, affecting the pairing system.[28] Carriers of this translocation are not affected by it, but they can experience difficulty reproducing. Mothers can suffer miscarriages or in case of survival, the fetuses are at high risk of birth defects and other abnormalities.[31] In the case of a family, two of three daughters suffered from intellectual and physical disabilities because they only inherited half of the mother's abnormal chromosomes and half of the father's normal chromosomes.[28] Because they did not inherit the two abnormal chromosomes from the mother, they were not chromosomally balanced, leading to birth defects.

If there is no presence of numerical or structural chromosome abnormalities, genetic mutations are another cause of birth defects. The most common mutations in genes include sickle-cell anemia, cystic fibrosis, Tay-Sachs disease, and Alzheimer's.[32] Recurring symptoms from patients with these mutations are frequent infections, respiratory complications, organ damage, loss of motor skills, and seizures, among others.[33] Genetic mutations take place during cell division when there is a mistake in replacing, removing, or adding codes that are not readable by the cells.[32] Germline mutations happen in the parent's reproductive cells and affect all the baby's cells, making the mutation hereditary. Somatic mutation occurs during the developing stage of the fetus and affects all the cells.[32]

It is commonly known that by the age of 40, a woman's chances of conceiving a pregnancy substantially diminish by 95%.[34] In contrast, a healthy 20-year-old typically has full capabilities to get pregnant and that makes their chances of conceiving higher.[35] Naturally, when the body gets older, the production of eggs decreases substantially. This, however, is not the only thing to consider when attempting to develop a baby around the age of 40. The chances of a miscarriage will also increase around this age due to the progressive negative chromosomal changes in eggs or oocytes.[36] Physicians have the

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ability to make tests of the ovarian reserve to determine the best way to go about the pregnancy or to advise individuals who want to go through pregnancy at that age.

Inbreeding causes the effect of overlapping DNA that results from the procreating of closely related biological partners that are related to the same common ancestors.[34] The excess amount of DNA typically is the cause of the permanent development of medical issues in the very early stages of fetus development. The chances of the infant being born with Autosomal recessive disorders like cystic fibrosis or sickle cell anemia are usually in response to the increased chances of both parents carrying the recessive genes that cause these diseases.[35] Historically, Royal families were commonly known to inbreed in their families to keep their blood "pure" by having consanguineous marriages.[36] This has been shown to have the outcome of many body deformities one of which is known as the Habsburg jaw. This facial deformity was present in the royal family of the Habsburgs who ruled Germany and Austria. The facial deformity was a result of a recessive pattern from the biological parents.

Complications During Labor

As a mother starts to go into labor, there are many factors that can delay the birth of the infant. While in labor, the women are getting continuous check-ups to make sure their blood pressure, glucose, and temperature is going smoothly and they are dilating properly. Some women may experience complications during their labor.

For instance, pre-eclampsia is a serious condition that occurs to the mother usually after the 20-week mark or even after birth that affects the blood pressure and other vital organs such as the kidneys provoking them to not function correctly. Some symptoms are present such as persistent headaches, trouble breathing, severe nausea, and changes in vision. This condition affects 5 to 8 percent of pregnancies and may even cause death.[37]

During labor, there are complications that occur such as the dilation process, amniotic fluid, and hemorrhaging. There can be complications with the dilation process, such as a prolonged latent phase, an arrest of dilation, or even precipitated dilation.[38] Others may experience the lack of being able to contract while in labor, prolonging labor delivery.[38] While the infant is in the womb, it must change its position to where its head is facing down towards the cervix, but at times, babies are in fetal malposition, making it difficult for the mother to push. The amniotic fluid plays an important role for the fetus because it is a liquid that revolves around the fetus that protects it from harm. The mother may lack or have too much of the amniotic fluid which is called Oligohydramnios and or Polyhydramnios.[37] Although there are many more complications that can occur during labor, all of them can affect the infant and the mother causing them to be in critical conditions or even death. Childbirth is taken with great precaution because things can take a turn quickly whether that be the birth moving quickly causing a dry birth to the birth going slowly to where the fetus excretes inside the mother.

Conclusion

It is asserted that detecting certain defects early on in the pregnancy during the baby's development would allow families to subject what care they would bring for the children. Learning the negative factors and maternal behaviors that cause birth defects can increase healthier baby development. What negative factors and maternal behaviors affect fetal development? A conclusion of certain circumstances that would negatively affect fetal development would be maternal negative behaviors such as alcohol, drugs, smoking, and diet, while negative factors are viruses, the influence of environment, genetics, age, and complications during pregnancy and labor.

Consuming alcohol during pregnancy develops FASD early on and consumption can affect child stunt growth. If a mother is to consume most types of drugs they are risking the possibility of labor miscarriages, premature delivery, cognitive developmental problems, abnormal brain structure, and fetal stress.[10] As previously stated, an AOG study concluded that smoking during pregnancy opens up the risk for bone fracture, asthma, and child respiratory infections. In a case where a mother would inject drugs through needles, there is a high risk of obtaining HIV. It is confirmed that if the maternal mother does get HIV, the possibility of the infection being passed down to children is extremely high.[12] A healthy diet is extremely vital in order to provide a steady pregnancy. In contrast to a healthy diet, a poor diet can increase anemia, preeclampsia, child stillborn, and the nervous system.[16] Including healthy meal plans and all nutrients is crucial because it strengthens infants' bones and teeth.[18] Viruses have also been a huge factor that may dictate negative fetal development. As described before, viruses have increased a child's

neurodevelopment by twice as much, as well as elevating the risk of ASD.[21]

Congenital anomalies and death have resulted in infants from viral infections.[29] In order for a pregnancy to run smoothly, a safe environment must be provided. In a violent situation, a pregnancy can negatively result in hemorrhage, preterm rupture of membranes, premature placental abruption, and low birth rate.[23] Although a safe environment is provided throughout the entire term, when the time comes to deliver the baby, it is crucial that the birth runs as smoothly as possible. Not doing so, can result in a critical condition or death in the mother or the infant. Genetically, occurrences like Down syndrome, heart defects, and palatal abnormalities have resulted. Providing accurate care and consideration for the mother and infant can reduce the risk of congenital defects.

Acknowledgements

Monica Betancourt-Garcia, MD, Program Director; Melissa Eddy, MS, Program Manager

Funding

Funded by DHR Health Institute for Research & Development; DHR Health; Region One ESC GEARUP College Ready, Career Set!; Region One ESC GEARUP College Now, Career Connected; Region One ESC PATHS; Region One ESC Upward Bound Math & Science; Benavides ISD; and Jubilee Academy-Brownsville

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