DHR Proceedings

Special Edition: Junior Clinical Research (2023), Vol. 3 No. S2
https://doi.org/10.47488/dhrp.v3iS2.86

COMMENTARY

What Environmental Factors Increase the Risk of Cerebral Palsy in Unborn Children?

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Received: June 29, 2023
Accepted for publication: September 1, 2023
Published: November 16, 2023

Introduction

Approximately 1 in 345 children are diagnosed with cerebral palsy and 85%-90% of these cases are congenital.[1] Cerebral palsy is a complex and multifaceted neurological disorder that has significant implications for individuals and their families. There are a wide range of risk factors that can contribute to the development of cerebral palsy, including environmental factors that can increase the risk of cerebral palsy in the fetus. Some of these risk factors are modifiable and can reduce the risk of cerebral palsy. By understanding the intricacies of cerebral palsy, we can contribute not only to medical advancements but also to improving the quality of life for those affected.

What is Cerebral Palsy?

Cerebral palsy is a motor disability that affects both brain development and muscle movement and is caused by brain damage which results from both physical complications and chemical impediment of the gestational process.[2] Children affected by cerebral palsy are very limited in mobility. Compared to other kids' abilities, children with cerebral palsy have an impairment of various physical and motor skills. Consequently, this can cause them to be prone to mental health conditions. Almost half (46%) of children with cerebral palsy have reported anxiety and depression, amongst other conditions.[3] Symptoms of cerebral palsy can range from minor to severe. While cerebral palsy is not a progressive disorder, these symptoms have the potential to change over time, making child development strenuous and burdensome.[2]

Maternal Diet and Medication Risk for Cerebral Palsy

Being cautious of what a mother ingests during pregnancy is crucial to the health of her baby. Studies have shown that certain diets and medications can have a big impact on an infant's brain development and can increase the risk for cerebral palsy.[4] Medications such as opioids and antibiotics should be used with caution.[5] An example of these mediations is betamethasone. Betamethasone is a drug given to pregnant mothers who are at risk of giving birth prematurely. However, administering more than one dose has been proven to cause damage to the white matter of the fetus's brain.[6] Another drug that many pregnant mothers take that could cause cerebral

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damage in the fetus is Pitocin. Pitocin is a drug given to mothers in labor to cause uterine contractions and speed up the birthing process. However, if given an incorrect dose, the contractions can become too powerful and cut off oxygen for the fetus, leading to brain trauma-induced cerebral palsy.[7] Diets and caloric intake have also been associated with gestational risk, with one study demonstrating how maternal obesity has an impact on infant health.[8] Alongside some drugs, certain vitamins and supplements have proven to increase the risk of a fetus developing cerebral palsy.[9] Protective nutrients such as those found in fish and folate should be considered for infant health and to decrease the risk for cerebral palsy.[9] Other nutrients, however, such as those found in meat, are considered a potential risk for cerebral palsy.[10] A study in Norway and Denmark looking at maternal intake found that mothers who supplemented with folate had a lower association for cerebral palsy.[8,9] Among births where the mother was diagnosed with obesity, her child had a higher risk of cerebral palsy. Studies show that out of 6.2 million births, 67,200 (1.1%) of recorded mothers had obesity and 8,798 (0.14%) of children born had cerebral palsy.[11] Keeping good nutrition during pregnancy can lower a child's risk of cerebral palsy. Physicians have recommended for pregnant women to avoid taking vitamin A during pregnancy, especially in the form of topical retinoids and other acne products. In fact, doctors always ask patients if they are pregnant before prescribing vitamin A based acne products to ensure that no harm is caused.[12] Studies have shown that mothers who have used retinoids and other vitamin A products during pregnancy have birthed babies with fetal retinoid syndrome and other neurodevelopmental impairments leading to cerebral palsy. Adequate maternal nutrition and health status is important for the growing fetus. If good nutrition is not present during pregnancy, it can lead to long term effects for both the mother and the baby.

Maternal Infection

Infections can cause the mother's immune system to increase the number of proteins called cytokines. Cytokines circulate in the blood and brain of the child, which can cause inflammation. Cytokines are signaled to repair and remodel tissue after certain cellular behavior. When cytokines bind to the receptors, they introduce hundreds of interferon (IFNs) and stimulated genes (ISGs).[13] These genes assist in the restriction of infections in the body. There are three types of IFNs, and they all have different functions and targets based on the expressions of the receptors. During pregnancy, the IFNs are employed and used in a defense against pathogens. The alterations that the IFNs induce can lead to pregnancy complications and congenital abnormalities. Since the influx of cytokines can cause congenital disorders, it can be concluded that IFNs pose a risk for cerebral palsy.[14]

The most common congenital infection is cytomegalovirus (CMV), which is found in 1% of live births.[15] CMV has been linked as a risk factor for the development of cerebral palsy. One study explored the relationship between the level of CMV infection and the developmental skills in children with cerebral palsy. Not only were a larger number of copies of CMV found in mothers of children with cerebral palsy compared to the control group, but decreased motor function and increased chance of spastic quadriplegia were also found throughout the group of cerebral palsy children with mothers of higher levels of CMV during pregnancy.[16] Although no relation was found between abnormalities of brain tissues and the amount of CMV in mothers, this study still supports the idea that CMV is a risk factor for cerebral palsy and the level of motor development the child will have.

Chorioamnionitis has also been linked to cerebral palsy. It is an infection of the placenta and amniotic fluid causing inflammation.[17] A case study of 231,582 infants with either spastic or dyskinetic cerebral palsy and a control group of children without cerebral palsy was conducted to determine if chorioamnionitis increases the risk of developing cerebral palsy. Fourteen percent of cases with cerebral palsy were diagnosed with chorioamnionitis, while only 4% of the control group were diagnosed with it. Other conditions found through logistic regression that may lead to cerebral palsy were intrauterine growth restriction and nulliparity.[18] Another study examined the relationship between chorioamnionitis, extra-amniotic infections, and the risk of cerebral palsy in children. Californian births between 1991 and 2001 with maternal hospital diagnoses of intra and extra amniotic infections up to 12 months before birth were studied. It was determined that an infection diagnosis was more common in mothers of children with cerebral palsy. Out of the 8,473 children with cerebral palsy, 7.6% of their mothers had a chorioamnionitis diagnosis, compared to only 2.0% of mothers of children without cerebral palsy.[19] The correlation between chorioamnionitis and cerebral palsy supports the claim that the amniotic inflammation from chorioamnionitis has an increased chance of damaging the fetal brain and leading to cerebral palsy.

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In addition to CMV and chorioamnionitis, maternal urinary tract infections have also been found to be a potential risk factor in children developing cerebral palsy.[20] A study done amongst 112 mothers of children with cerebral palsy and a control group of 153 mothers of children without cerebral palsy found that 17.9% of mothers of children with cerebral palsy had a UTI, while only 5.2% of mothers in the control group had UTIs during pregnancy.[21] At the time of the study, not much previous research had identified a relationship between maternal UTIs and the risk for cerebral palsy, making both this study and Polivka et al., 1993 one of the first to report detecting an association between UTIs and cerebral palsy. Another study found a similar relationship between mothers with UTIs and the birth of children with cerebral palsy. An analysis of 8,473 mothers of infants with cerebral palsy found that 5.2% had been diagnosed with a UTI, compared to 3.1% of 6,010,031 mothers of children without cerebral palsy.[22] It is important that healthcare professionals aim to educate pregnant patients and improve patient care to prevent such a common infection like a UTI from occurring, thus preventing harm to fetal brain development and preventing cerebral palsy.

Chemicals and Toxicity

Interactions between environmental chemicals and fetal development may also increase the risk of cerebral palsy and create hormonal imbalances.[23]

Methylmercury, a teratogen found in the bodies of fish and sea-dwelling consumers, can be spread through the biomagnification of food chains.[24] The concentration of methylmercury increases directly with the trophic level, meaning humans who consume seafood are exposed to the chemical. Methylmercury exposure would not be problematic unless consumed in large amounts to the average person, however, to the fetus, it is more susceptible to the effects of toxic chemicals and teratogens.[25] Cerebral palsy is one of the various malformations caused by developmental impairment associated with methylmercury exposure. In areas like the Great Lakes, there have been higher incidences of cerebral palsy hospitalization, indicating a correlation between seafood consumption in an area known for high methylmercury levels and the occurrence of cerebral palsy.[26]

Pesticides are one of the most acknowledged causes for endocrine disruption in humans.[27] Of the various effects on the human body, disruptions in the fetus during gestation have been related to proximity of agricultural areas in which pesticides were used. In multiple studies with thousands of controls, mothers who resided near agricultural operations were reported to have higher incidence of cerebral palsy.[28]

Although the knowledge of lead's neurodegenerative effects is widely recognized (for example, it's phasing out of gasoline as an engine stabilizer and as an ingredient in paint), industrial factors as well as the removal of lead-containing objects still allow lead to be a serious problem in the neurodevelopment of children.[29] Through the removal of paint that was originally applied with lead as an ingredient, as well as the demolition of lead-containing buildings, lead dust can be released into soils, recreational products, and water. Mothers near mining operations involving the harvesting of lead can also put children at risk for stunted neurodevelopment, as well as higher lead absorption.[30] In areas of limited access to drinking water regulation, studies have shown that children with cerebral palsy have higher concentrations of lead.[31]

Conclusion

Research on the relationship between environmental factors and cerebral palsy has elucidated various factors that can contribute to the increased risk of cerebral palsy. These factors include being exposed to an illness while pregnant, taking certain medication, and being exposed to certain toxins. More importantly, some of these risk factors are modifiable and it is crucial for expecting mothers to limit their interaction with these risk factors. By taking action to lessen exposure to these environmental factors, we can contribute to the prevention of cerebral palsy.

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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