Maternal occupational exposures associated with the onset and progression of childhood leukemia

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INTRODUCTION

Leukemia is the most commonly diagnosed and the most common cause of cancer death in children worldwide. The two main types of acute leukemia are acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), with ALL affecting 80% of childhood leukemia cases (Ciesielska et al., 2024). ALL involves the uncontrolled growth of lymphoblasts, which are lymphocyte precursor cells. When lymphoblasts excessively proliferate, the body experiences a drop in the production of bone marrow cells, anemia, thrombocytopenia, and /or neutropenia due to low white blood cell count(Wartenberg et al., 2008). Some of the most common symptoms experienced by ALL patients are fatigue, bruising, hepatomegaly, splenomegaly, and lymphadenopathy, and infections (Ciesielska et al., 2024). Late and long-term impacts of leukemia treatment options, which are becoming more effective and widespread, on survivors include second cancers, heart and lung problems, learning issues, changes to growth and development, fertility issues, and bone problems (Living as a Childhood Leukemia Survivor, n.d.).

An increasing number of research studies on childhood leukemia indicate that environmental hazards may play a role in the development of childhood leukemia(Metayer et al., 2016). One specific type of environmental hazard is an occupational exposure, which is defined as contact with a potentially harmful biological, chemical or physical substance due to an individual's duties at work (Occupational Exposure | NIH, n.d.). A specific and under-researched type of occupational exposure is that experienced by pregnant women. Research shows that the development of childhood ALL may be linked to a mother’s exposures during pregnancy, which is why it's important to explore the association between maternal occupational exposures and childhood leukemia in greater detail (Schüz et al., 2000).

During pregnancy, blood volume increases while hemoglobin and platelet concentrations decrease due to dilution (Vinnars et al., 2023). Chemical metabolism is also altered due to increased nutritional and metabolite demands of the fetus and other physiologic and pathologic changes associated with pregnancy such as hyperemesis, increased glomerular filtration rate, and altered hepatic function due to increased blood flow (Vinnars et al., 2023). Pregnant workers also typically have suppressed immune responses and decreased lung vital capacity, which have similar implications in terms of what their bodies can chemically tolerate (CDC, 2024). Additionally, due to the smaller size and rapid development of unborn babies, certain chemical exposures are more dangerous for them than they are for adult workers. Fetuses are undergoing rapid cell division as they grow and develop, which makes them more susceptible to errors in the cell division process in response to any toxin exposures (Vinnars et al., 2023). Additionally, fetal development depending on the trimester is a key time where neurodevelopment, reproductive development, and metabolism development occurs in response to endocrine and hormonal signals from the mother. Disruptions to these endocrine axes during development make them more susceptible to harm than adult workers with fully developed organ systems and hormonal axes (Vinnars et al., 2023). Unfortunately, little research has been done so far on what concentrations or exposure levels can be tolerated

by fetuses due to ethical implications as well as significant variability in fetal metabolism based on gestational age and size. Thus, unborn children may be at even higher risk of occupational exposure-based diseases than most realize.

Notably, high family income and parental educational levels are associated with a lower overall risk of childhood leukemia(Hashemizadeh et al., 2013). A potential reason for this disparity is that low income occupations often involve high exposure to certain occupational hazards (Ingram et al., 2021). Therefore, low income groups may be disproportionately impacted by childhood leukemia due to disparities in occupational exposures during the pre-conception, pregnancy, and childhood periods. Stricter legislative regulation of workplace safety measures is needed to reduce the disparity in childhood leukemia in low income populations.

OCCUPATIONAL EXPOSURES AND CHILDHOOD LEUKEMIA

Research revealing the association between various maternal occupational exposures and the development of childhood leukemia are stressing the need for stricter regulation surrounding occupational exposures. Multiple systematic reviews and meta-analysis studies have found an association between maternal occupational exposure to pesticides and childhood leukemia specifically, with the relationship being especially strong when the pesticide exposure was farm-related (Van Maele-Fabry et al., 2010; Wigle et al., 2009). This suggests that a pregnant woman holding a low-income occupation as a farmer could significantly increase the risk of her unborn child developing childhood leukemia. Research has revealed a link between occupational pesticide exposure both before and during pregnancy and an increased risk of childhood leukemia. This underscores the importance of implementing protective measures at all times—not just during pregnancy—to minimize the risk of childhood ALL. Associations were also found between maternal occupational exposure to herbicides and insecticides and childhood leukemia, but there are far fewer studies discussing this relationship. More research is needed in this specific area. (Wigle et al., 2009)

A group of studies conducted in the United States also found an association between maternal occupational exposure to paints/lacquers during the preconception and index pregnancy periods and increased risk of childhood ALL (Schüz et al., 2000). A comprehensive meta-analysis of epidemiologic studies found a similar association with paint, but also with solvent and petroleum during pregnancy specifically (Zhou et al., 2014). A population-based case control study found that children whose mothers were occupationally exposed to extremely low frequency magnetic fields during pregnancy had greater risk of developing leukemia (Infante-Rivard & Deadman, 2003). One of the professions with the highest level of exposure to extremely low frequency magnetic fields is a sewing machine operator (Infante-Rivard & Deadman, 2003), which further demonstrates the need for increased preventive measures and policies to protect pregnant women, especially low-income pregnant women, and their children. Thus, a growing body of research studies are demonstrating that maternal exposure to pesticides, paints and solvents, and extremely

low frequency magnetic fields are linked to the development of childhood leukemia and suggest the need to have stricter regulations introduced and enforced in workplaces. These may include OSHA laws such as stricter regulation of appliances that emit low frequency magnetic fields at the manufacturer level, laws requiring workplace monitoring and occupational exposure limits, and requirements for employers to provide protective gear for higher risk jobs (US EPA, 2023). Additionally, other possible actions may be based on laws passed by the EPA for environmental exposure protection, for example bans on certain carcinogenic chemicals, requiring worker training and exposure notification requirements, and web-based tools to help workers understand their exposure and risks (US EPA, 2023).

EXPOSURE TIMING

Exposure timing may also play a big role in development of childhood leukemia via maternal occupational exposures. For example, neonatal blood sports that have been used to identify chromosomal translocations involved in leukemia have suggested that ALL starts in the uterus (Heck et al., 2019). Furthermore, some hypothesize that childhood leukemia is initiated via a prenatal primary event and can be further developed as a result of a postnatal second event(Van Maele-Fabry et al., 2010). Examples of prenatal primary events include exposures before conception and/or during pregnancy while examples of postnatal second events include mother and child exposures after birth as well as exposures that arise from breastfeeding (Van Maele-Fabry et al., 2010). Although researchers have yet to define a specific exposure timing window during which childhood leukemia is most likely to develop, it's critical to target not only the time period of the actual pregnancy, but also the pre-conception period as well as the neonatal/early childhood period with preventive regulations in the workplace in order to prevent maternal occupational exposures from contributing to the prevalence of childhood leukemia in low-income populations (Van Maele-Fabry et al., 2010). In order to reduce prenatal exposure to toxic environmental agents, the American College of Obstetricians and Gynecologists recommends participating in clinical encounters, especially since toxic environmental agents often disproportionately impact the health of underserved populations (American College of Obstetricians and Gynecologists' Committee on Obstetric Practice, 2021). As mentioned previously, the windows before and after pregnancy are also crucial to consider, so the same might be advised to those hoping to have children in the future as well as those who recently had children. Although this alone is not enough to eliminate the leukemia disparity experienced by pregnant low-income workers, it is a step in the right direction to reduce these disparities in conjunction with stricter workplace regulations and monitoring to protect this vulnerable group.

CONCLUSION

According to the National Institute for Occupational Safety and Health, which is a part of the Centers for Disease Control and Prevention's Department of Health and Human Services, most occupational exposure guidelines and limits were determined based on studies involving non-pregnant adults, which suggests that the interventions and preventive strategies

in place may not protect a pregnant person and her fetus adequately (CDC, 2024). For example, some hazardous materials may be absorbed more readily by a pregnant woman than someone who is not pregnant, meaning that the lethal exposure levels may differ (Vinnars et al., 2023). Due to the physiologic changes that occur during pregnancy to optimize fetal growth and development and prepare the body for delivery, pregnant women may be more susceptible to the effects of toxic exposures (Vinnars et al., 2023). A current intervention helping to reduce the impact of maternal occupational exposures on the development of childhood leukemia include the Pregnant Workers Fairness Act, which requires employers to make accommodations for employees who have limitations related to pregnancy or childbirth (The Pregnant Workers Fairness Act, n.d.). Although this legal intervention is undoubtedly helpful in reducing maternal occupational exposures, it fails to address the risks that can come with pre-conception exposure to occupational hazards. Overall, these gaps in workplace interventions suggests the need for more occupational intervention studies specifically targeted at maternal exposures. Although there has been an increase in the number of intervention studies investigating chemical exposures in workplaces, the quality of studies is still low and not as comprehensive as they need to in order to incite actionable change (Ohlander et al., 2020). We need to see a legislative call to action requiring higher quality studies directed specifically at maternal exposures so that stricter regulation of workplace safety measures can be enforced and the disparity of low income groups being disproportionately impacted by childhood leukemia due to disparities in occupational exposures during the pre-conception, pregnancy, and childhood periods can be rectified.

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