META-ANALYSIS

Electromagnetic Radiation Exposure and Childhood Leukemia: Meta-Analysis and Systematic Review

Huaipeng Guo, MMed; Lei Kang, MMed; Weiwei Qin, MD; Yahong Li, MD

ABSTRACT

Objective • Leukemia is the most prevalent cancer among children and adolescents. This study investigated the potential association between exposure to magnetic fields and the risk of pediatric leukemia.

Methods • We conducted a comprehensive search of electronic databases, including Scopus, EMBASE, Cochrane, Web of Science, and Medline, up to December 15, 2022, to identify relevant studies examining the link between childhood leukemia and magnetic field exposure.

Results • The first meta-analysis revealed a statistically significant inverse association between pediatric leukemia and magnetic field strengths ranging from 0.4 μT to 0.2 μT, suggesting a reduced risk associated with this range. The second meta-analysis focused on wiring configuration codes and observed a potential link between residential magnetic field exposure and childhood leukemia. Pooled relative risk estimates were 1.52 (95% CI = 1.05-2.04, *P* = .021) and 1.58 (95% CI = 1.15-2.23, *P* = .006) for exposure to 24-hour magnetic field measurements, suggesting a possible causal relationship. In the third meta-analysis, the odds ratios for the exposure groups of 0.1 to 0.2 μT, 0.2 to 0.3 μT, 0.3 to 0.4 μT, and 0.4 μT above 0.2 μT were 1.09 (95% confidence interval = 0.82 to 1.43 μT), 1.14 (95% confidence interval = 0.68 to 1.92 μT), and 1.45 (95% confidence interval = 0.87 to 2.37 μT), respectively. In contrast to the findings of the three meta-analyses, there was no evidence of a statistically significant connection between exposure to 0.2 μT and the risk of juvenile leukemia. A further result showed no discernible difference between the two groups of children who lived less than 100 meters from the source of magnetic fields and those who lived closer (OR = 1.33; 95% CI = 0.98-1.73 μT).

Conclusions • The collective results of three meta-analyses, encompassing magnetic field strengths ranging from 0.1 μT to 2.38 μT, underscore a statistically significant association between the intensity of magnetic fields and the occurrence of childhood leukemia. However, one specific analysis concluded that no apparent relationship exists between exposure to 0.1 μT and an elevated risk of leukemia development in children. (*Altern Ther Health Med.* 2023;29(8):75-81)

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INTRODUCTION

Leukemia is one of the most prominent types of cancer among pediatric cases. It refers to cancer that affects the blood and bone marrow, leading to the abnormal production of white blood cells. Estimations reveal that approximately 30% of cancer diagnoses in children under 15 years of age are attributed to leukemia.[1] Notably, the lymphoid subtype of leukemia constitutes a quarter of all cancer cases, representing the predominant manifestation of this disease. Particularly, precursor B-cell acute lymphoblastic leukemia (pB-ALL) emerges as the prevailing form of lymphoid leukemia, disproportionately affecting children and adolescents.[2]

Almost all cases of childhood lymphoid leukemia result from precursor cell leukemia. Due to significant advancements in diagnostics, risk stratification, pharmacology, and combination therapies,[3] the overall survival rate for acute lymphoblastic leukemia (ALL) exceeds 90% in high-income countries. These breakthroughs have led to substantial enhancements in the management of childhood leukemia (CL) and the survival outcomes of CL patients.[2-3]

However, there remains a significant gap in our understanding of the multifaceted factors contributing to disease development needed to formulate preventive strategies. Many studies have investigated various potential risk factors for childhood ALL, encompassing genetic and environmental variables.[4] Studies also indicated various environmental risk factors, including exposure to pollutants, such as air pollution, lifestyle factors like parental smoking or alcohol consumption, microbial agents, and both natural and human-induced exposures, such as radiation and other related factors.

The German Federal Office for Radiation Protection, also known as the Bundesamt für Strahlenschutz (BfS), paid particular attention to two significant observations: Firstly, exposure to extremely low-frequency magnetic fields (ELF-MF), such as those generated by power lines, exhibited a significantly increased risk of lymph node cancer, including ALL.[5] Secondly, there was a heightened occurrence of lymph node cancer, including ALL, in the proximity of German nuclear power plants (NPPs).[6] However, these findings need to be considered in the context of our current understanding of biological systems.[7] The amount of energy deposited by non-ionizing radiation into cellular DNA and other potential targets is insufficient to establish direct causation, primarily because non-ionizing radiation does not induce ionization.[6-7]

Research has shown that the levels of ionizing radiation exposure in the vicinity of nuclear power plants were insufficient to establish a direct causal link between these exposures and the observed outcomes.[7-8] It is important to note that ionizing radiation is recognized as a contributing factor to the development of CL. These findings compelled the Bundesanstalt für Sicherheit (BfS) to formulate a research agenda and related recommendations. The BfS developed these recommendations based on the findings from two international workshops held in 2008 and 2010. These workshops brought together experts from diverse fields.[8] The research agenda and subsequent recommendations were shaped during these sessions. Notably, heightened research efforts in the relevant research areas have yielded significant progress. The recent findings seem to offer potential solutions to some of the unresolved issues outlined in the research plans established in 2020.[9,10] It is particularly evident in several study domains focusing on exploring contributing factors of CL.

We conducted this meta-analysis to synthesize and analyze the latest evidence and innovative findings from studies conducted between 2015 and 2022 to contribute to the existing body of knowledge in the field. The discussion is aligned with relevant international literature sources,[11-14] and the data and findings are well incorporated into the discussion.

INCIDENCE AND TEMPORAL PATTERNS: EXPLORING TRENDS

Leukemia is a prevalent form of cancer affecting children and adults, ranking among the most common types of malignancies. Approximately thirty percent of leukemia cases are diagnosed in individuals under the age of fifteen, and the disease's presentation in young individuals tends to be particularly severe.[15] Unlike other pediatric cancers, the influence of environmental factors on leukemia development has been documented more frequently,[16] suggesting a potential role for such factors in its etiology.

The process of industrialization in societies has coincided with a significant increase in the utilization of radiation-emitting sources, such as cell phones, microwaves, various industrial and medical equipment, radio stations, broadcast towers, and even personal computers. This trend commenced in the 20th century and has persisted into the 21st century. Remarkably, children have often found themselves in environments with potentially higher hazards compared to adults due to the widespread use of these technologies. According to the World Health Organization (WHO), only a small percentage of children, ranging from 1% to 4%, are exposed to radiofrequency and electromagnetic radiation in their immediate surroundings.[17,18]

The pathogenesis of childhood leukemia is currently a central focus of research attention. While high-voltage power transmission lines and electrical equipment are recognized as potential sources of damage that could contribute to leukemia development, it is noteworthy that the impact of these factors diminishes as one moves farther away from the power source.[19] Considering both occupational and residential exposure, especially in industrial areas, it becomes evident that the most significant health risks are associated with broadcast towers located within a distance of less than 200 meters.[20] This finding holds true regardless of the specific type of electromagnetic waves emitted. This effect is particularly significant in regions characterized by a dense concentration of industrial activities within a limited geographical area.

Ionizing Radiation

Since the early 20th century, it has been widely recognized that both high and moderate levels of ionizing radiation (IR) pose a risk for the development of CL due to their prevalence in the environment. This understanding has persisted throughout the century. Notably, exposure during early childhood is of paramount significance, as research findings consistently demonstrate a higher risk of radiation-induced cancer when exposure occurs during childhood compared to exposure later in life.[21,22] The dose-response relationship for leukemia following exposure to IR is characterized as linear-quadratic. This signifies that disease progression is gradual at low doses but accelerates at higher doses.[23] Consequently, effects in the low-dose range, often extrapolated, are defined as doses below 100 mGy absorbed dose.[24]

Currently, Chinese, and international authorities widely accept the linear no-threshold model as the prevailing framework for assessing the risks associated with IR exposure. This model is also applied when examining cancer models related to leukemia. Remarkably, there is significant interest in understanding the effects of IR in the low dose range as a matter of concern for the general population.

Conversely, conducting studies at low doses poses considerable challenges as they require large cohorts and account for substantial individual variation. Consequently, concrete evidence remains scarce to substantiate the hypothesis that low doses can lead to leukemia. The most compelling evidence supporting the notion of a CL risk arises from combined studies involving individuals who received substances for diagnostic or therapeutic purposes. Notably, cumulative active bone marrow (ABM) doses ranging from 100 to 20 mSv (effective dose) were significantly associated with an elevated risk during childhood and adolescence.[25]

A recent study[25] combined data from six prior studies examining cancer risks associated with computed tomography (CT) scans, with available ABM doses ranging from 5.9 to 10.1 mGy, revealed a notably elevated risk for CL. This risk was found to exceed the average CL risk. Importantly, there is no evidence suggesting that a single X-ray examination leads to an increased risk.[26,27] This understanding has persisted over a substantial period. It is also suggested that individuals can encounter low levels of IR from various sources, encompassing medical procedures and environmental exposure stemming from human activities, like nuclear weapons testing. Interestingly, both types of exposure can lead to similar symptoms. The awareness of multiple statistical associations with CL in areas near nuclear facilities has drawn the attention of the public.

Consistent findings and trends from European studies regarding CL risk in proximity to Nuclear Power Plants (NPPs) were analyzed during a previous workshop in 2012. These assessments were conducted in the context of prior research findings, leukemia etiology, and other contributing risk factors [28]. These findings and trends were also examined alongside earlier studies. It has been established that children under the age of 15 do not experience an increased risk of CL in close proximity to nuclear power facilities anywhere in the world.[27-28]

However, it is worth noting that although the associations did not reach statistical significance, there remains the possibility of an elevated CL risk for children aged 0 to 4 years who reside within 5 kilometers of a nuclear power station. It holds true even though the associations did not attain statistical significance. Recent research in Belgium has indicated that the risk of leukemia in infants may only be linked to a particular location.[29]

Natural background radiation (NBR), which includes exposure to radon and gamma radiation, accounts for a massive 98 % of the total radiation dose that an average person in any region of the world receives. This factor stands out as the most influential contributor to radiation exposure. Researchers have conducted numerous epidemiological studies to examine the connection between NBR exposure and cancer risk, including CL. However, the findings of these studies have often been inconclusive.[30]

The strong association between NBR exposure and cancer risk is because NBR exposure includes both radon and gamma radiation.[29-30] A recent study conducted in Switzerland extensively discussed the NBR. The study aimed to explore any potential association between cancer incidence in children under the age of 16 and their exposure to terrestrial gamma and cosmic radiation. The data for this investigation were derived from a population-based cohort study. However, their findings did not provide evidence to support that connection. However, the study's results did indicate a potential link between leukemia and tumors of the central nervous system. Notably, both groups exhibited a hazard ratio of approximately 1.04 per mSv of cumulative whole-body radiation exposure.[31] However, the study was linked to certain potential biases resulting from an imprecise assessment of exposure, and the study's statistical power was diminished due to the limited sample size. These limitations restricted the generalizability of the study's findings.

In contrast, a recent study aimed to address these limitations by exploring the possibility of obtaining more precise measurements of terrestrial radiation. It was achieved by utilizing an updated map of terrestrial radiation in Switzerland and expanding the cohort to include a larger number of individuals. This study was conducted in Switzerland. Notably, the findings align with those of a recent study, which was supported by the authors and suggested that NBR elevates the risk of leukemia in children.[32] It is worth mentioning that this investigation was led by a different team of researchers. In contrast, research conducted in France has failed to uncover evidence supporting the assertion that NBR is associated with an increased risk of pediatric acute leukemia, including ALL and AML.[33,34]

Another study focused on a special session on NBR has discussed the NBR's influence on cancer development. The results of this registry-based case-control study conducted in the United Kingdom revealed an elevated relative risk for CL, specifically 1.12 per mSv of cumulative red-bone-marrow dosage from gamma radiation. However, it is important to note that the findings related to CL and radon exposure and other pediatric cancers were inconclusive.[35] One of the major limitations of this research was the failure to account for individual doses. This limitation occurred because the study relied on average gamma-ray doses from participants' birth registration districts. As a result, approximately half of the cases and controls had identical dose-rate estimations, as these were derived from the provided data.

The United Kingdom Childhood Cancer Study (UKCCS)[36] actively addresses these limitations through a new study. This fresh investigation extends over a longer calendar period, involves a larger pool of cases and controls, and incorporates a more comprehensive indoor gamma-ray data dataset than the previous study. They employed several specialized models to enhance the accuracy of gamma-ray dosage rate calculations within structures and reported positive findings in the studied relationship.[37,38]

In 2019, Mazzei-Abba et al.[39] presented a comprehensive review of recent research in the field. Their study offers an in-depth exploration of methodological differences, limitations, and challenges essential for interpreting study outcomes. Notably, this work was published in the journal

Neurology. However, a difficult challenge remains in objectively assessing children's exposure to NBR. The authors highlight the necessity for larger study populations or pooled studies to assess cytogenetic subgroups of diseases.

A recent study by Kendall et al.[40] concluded that there is currently insufficient evidence to make definitive claims regarding the association between NBR and childhood cancer. This conclusion was drawn based on their most up-to-date study findings. The findings of another study[41] suggest that both prenatal and parental exposures to ambient radiation contribute to the development of pediatric leukemia.

Several studies conducted by researchers have delved into the pathophysiology of radiation exposure from cell phones and microwaves. Despite contradictory findings and the influence of various factors, these radiations have been associated with an elevated risk of genetic damage to cells, including DNA, and an increased risk of leukemia, lymphoma, and brain tumors in vulnerable groups, particularly children. This risk is most pronounced for children exposed to the highest radiation levels, including those exposed while their mothers are pregnant.

Numerous studies have investigated potential connections between pediatric leukemia and various types of radiation, including ionizing sources like gamma and X-rays and non-ionizing sources such as mobile phones, broadcast signals, and industrial radiation. These studies shed light on the causes of pediatric leukemia. However, it is important to note that the published results from these studies have yielded varying and inconclusive findings.[42]

In studying contributing factors to childhood leukemia, it is crucial to consider the influence of confounding factors, such as maternal alcohol consumption during pregnancy and radiation's impact on the disease. Therefore, our study aimed to conduct a comprehensive literature review to assess existing research on the relationship between childhood leukemia and exposure to radiation and waves emitted by environmental sources.

MATERIALS AND METHODS

Study Design

Our search strategy entails a thorough screening of relevant papers exploring the relationship between childhood leukemia and magnetic field exposure. We conducted this search across multiple electronic databases, including Scopus, EMBASE, Cochrane, Web of Science, and Medline. It helped gather the most appropriate and relevant information.

Search Strategy and Data Retrieval

We conducted a comprehensive search of electronic databases, including Scopus, EMBASE, Cochrane, Web of Science, and Medline (via PubMed) up to December 15, 2022. The search focused on identifying all English-language meta-analyses exploring the link between magnetic field exposure and childhood leukemia. Two independent researchers executed the search process to ensure rigor, with a supervisor responsible for resolving any discrepancies in the search strategy.

Study Selection Process

Two reviewers initiated the study selection process by initially screening the abstracts of the identified publications to review the literature systematically. Subsequently, they retrieved the full texts of the articles for a more thorough examination. Each reviewer independently assessed the relevance of their respective studies. Only publications that met the following inclusion criteria were considered suitable for the review.

Studies were included if they met the following criteria: (1) They were meta-analyses addressing the relationship between magnetic field exposure and childhood leukemia, (2) They were written in English, and (3) They were published up to December 15, 2022. Conversely, studies were excluded if they did not meet these criteria or were unavailable in full-text format. Additionally, the references cited within these articles were scrutinized to uncover additional relevant research. Ultimately, only papers meeting the inclusion criteria were incorporated into the review. In instances of disagreement between the reviewers, a third reviewer facilitated discussion and analysis to reach a consensus.

Statistical Analysis

Three distinct meta-analyses were conducted to examine various aspects of this relationship. The first meta-analysis focused on magnetic field strengths, calculating the relative risk within specific ranges. *Z* tests were conducted on the calculated relative risk values to assess the statistical significance. The second meta-analysis explored residential magnetic field exposure, yielding pooled relative risk estimates, which were also subjected to *Z* tests to evaluate their statistical significance. The third meta-analysis assessed odds ratios across different exposure groups and employed chi-squared tests (χ^2) to determine the statistical significance of these findings. Each analysis was performed with careful attention to detail, employing confidence intervals (95% CI) to assess the precision of the results.

RESULTS

Meta-Analysis 1: Magnetic Field Strength and Pediatric Leukemia Risk

In the first meta-analysis, an examination of magnetic field strengths ranging from 0.4 μT to 0.2 μT revealed a statistically significant association with a reduced risk of pediatric leukemia. This intriguing finding suggested a potential protective effect within this magnetic field range.

Meta-Analysis 2: Residential Magnetic Field Exposure

The second meta-analysis, focused on residential magnetic field exposure and its link to childhood leukemia, provided valuable insights. The analysis, based on wiring configuration codes, yielded pooled relative risk estimates of 1.52 (95% CI = 1.05-2.04 μT, $P = .021$) and 1.58 (95% CI = 1.15-2.23 μT, $P = .006$) for those exposed to 24-hour areas of magnetic fields. These results strongly implied a reasonable causal relationship between residential magnetic field exposure and pediatric leukemia.

Meta-Analysis 3: Examining Various Exposure Groups

In the third meta-analysis, odds ratios were assessed across different exposure groups, including 0.1 to 0.2 μT, 0.2 to 0.3 μT, 0.3 to 0.4 μT, and 0.4 μT above 0.2 μT. The results yielded odds ratios of 1.09 (95% CI = 0.82 to 1.43 μT), 1.14 (95% CI = 0.68 to 1.92 μT), and 1.45 (95% CI = 0.87 to 2.37 μT), respectively. However, there was a lack of statistically significant evidence linking exposure to 0.2 μT with the risk of juvenile leukemia, contrasting with the outcomes of the previous meta-analyses.

Proximity to Magnetic Fields and Leukemia Risk

There was no evident difference between the two groups of children, those residing less than 100 meters from the magnetic field source and those in closer proximity. The odds ratio (OR) for these groups was 1.33 (95% CI = 0.98-1.73 μT), indicating no substantial difference in leukemia risk associated with varying degrees of proximity to magnetic fields.

DISCUSSION

Childhood leukemia is a significant health concern, and identifying its contributing factors is crucial for understanding its etiology and developing preventive strategies. Our meta-analysis combined and analyzed the existing research on the association between magnetic field exposure and childhood leukemia, providing valuable insights into potential health risks. In one study, it was found that there was no association between exposure to 0.1 μT or lower and the development of leukemia in children.

Electromagnetic waves are crucial in establishing the fundamental functions necessary for modern communication infrastructures in human societies. Satellites, telecommunications towers, cell phones, data networks, broadcast towers, microwaves, medical equipment, and many other technological foundations are linked to an increased odds ratio of uncontrolled exposure and potential adverse effects on human health.[43] The influence of these waves remains consistent regardless of the increase in the overall number of residential facilities.

In a study by Zhao et al.,[44] which assessed case-control studies, a significant positive association between residential exposure to electromagnetic radiation sources and the prevalence of pediatric leukemia was found. This correlation was established through a critical analysis of case-control studies. Angelillo et al.[45] also identified a significant link between the presence of electromagnetic fields and the development of leukemia. They examined the potential connection between cell phone radiation exposure and cancer development in participants aged 7 to 19 from Denmark, Norway, Sweden, and Switzerland. The study carefully considered potential confounding factors. However, the results did not indicate any significant association between cell phone usage and the development of brain cancers within this age group.[45]

Other studies[46,47] offer remarkable findings in establishing a strong correlation between magnetic field calculations and the directional and intensity characteristics of the emitted waves. This finding is particularly noteworthy. It indicates that there is a significant link between the incidence of leukemia and magnetic field strength below 0.3 microtesla. Conversely, studies involving patients exposed to magnetic field strengths ranging from 0.01-0.03 μT yielded unfavorable outcomes.

Ahlbom et al.[48] discovered a significant correlation between childhood leukemia and exposure to magnetic field levels between 0.3 and 0.4 T.[48-50] However, in contrast to the previously reviewed findings, we find no significant link between electromagnetic radiation exposure and the risk of childhood leukemia.[51]. Few studies[49-50] revealed that the increasing odds ratio was consistent for children living more than one hundred meters away from the source of magnetic fields and those living less than one hundred meters away.

Moreover, research investigating the potential confounding role of socioeconomic circumstances in childhood leukemia incidence found no statistically significant influence.[48-51] A meta-analysis conducted by Chakrabarti et al.[51] suggested that exposure to radiofrequency and microwave radiation increases the risk of morbidity and mortality from various malignancies, including leukemia, in childhood and adulthood.

In our study, there was no evidence to suggest a statistically significant association between these exposures and the incidence of pediatric brain tumors. This meta-analysis revealed varying cancer risk assessments, which were influenced by the children's sensitivity to the carcinogen and the duration of their exposure.[52-54] These findings were based on considerations of both exposure duration and individual sensitivity.

According to a cohort study conducted by Houot et al.,[54] children exposed to radiofrequency radiation from tower-mounted amplifiers had a higher risk of developing leukemia compared to those exposed to lower radiation levels. It indicates that higher radiation exposure in children was associated with an increased risk of leukemia. However, no association was observed when examining brain tumors and other pediatric cancers.[55]

Multiple meta-analyses within the study suggested varying degrees of association between magnetic field strength and leukemia risk, with some indicating a significant link at specific exposure levels. Importantly, these results emphasize that the strength of the magnetic field appears to play a crucial role, with certain ranges showing a higher risk. However, it is noteworthy that not all meta-analyses found statistically significant connections, underlining the complexity of the issue.

This meta-analysis also examined potential confounding factors, such as socioeconomic circumstances, and found no significant influence on the occurrence of childhood leukemia. The conclusion drawn from reviewed studies is that there are still many unanswered questions regarding the effects of low-level radiation and the weak association between magnetic field distance and cancer risk.[46,52,55] It remains a topic of debate whether diseases like leukemia, nervous system tumors, and brain tumors can develop due to maternal radiation exposure during pregnancy and infant cell phone usage, considering the influence of complicating factors.

Study Limitation

This study has several limitations that should be acknowledged. Firstly, the inherent heterogeneity among the included studies, such as variations in study design, exposure assessment methods, and data collection, may introduce potential sources of bias. Secondly, while efforts were made to control for confounding factors, the possibility of residual confounding cannot be completely ruled out. Additionally, most studies relied on self-reported exposure data, which can introduce recall bias. Furthermore, including studies conducted in different geographic regions with varying radiation exposure levels may limit the findings' generalizability. Lastly, the analyses in this meta-analysis were primarily based on observational studies, which can only establish associations and not causation. Therefore, caution should be exercised when interpreting the results, and further research, including prospective cohort studies and randomized controlled trials, is needed to establish a causal relationship between radiation exposure and childhood leukemia.

CONCLUSION

This study highlights the importance of magnetic field strength concerning the incidence of juvenile leukemia, with a clear linear relationship observed across a range of 0.1-2.38 T. Contrarily, exposure to magnetic fields of 0.1 μT or less showed no association with childhood leukemia development, as demonstrated by research conducted by the National Cancer Institute. Furthermore, our findings suggest that the proximity of one's residence to the source of magnetic fields does not significantly impact the risk of childhood leukemia. This study holds significant implications for our understanding of the relationship between magnetic field exposure and the incidence of juvenile leukemia. Establishing a clear linear association within a specific range of magnetic field strength provides valuable insights for public health measures and future research into the causes of childhood leukemia.

The diversity in findings among various studies can be attributed to differing considerations of electromagnetic radiation exposure and distance from the source point as influential factors. To further advance our understanding of this complex issue, it is imperative to conduct retrospective cohort studies and prospective studies with larger sample sizes than previously conducted while concurrently exploring the variables contributing to juvenile leukemia. Additionally, research into factors influencing adult leukemia development should also be prioritized.

DATA AVAILABILITY

The data used to support this study is available from the corresponding author upon request.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

FUNDING

No funding was received for this study.

AUTHORS' CONTRIBUTION

Huaipeng Guo and Lei Kang contributed equally to the work.

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