

Research

Exploratory case–control study on childhood cancer near the Mar Menor lagoon Region of Murcia (Spain) 2000 to 2018

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Abstract

The Mar Menor, Europe's largest saltwater lagoon in the Mediterranean basin (Murcia, southeastern Spain), is an ecosystem facing severe pollution, anoxia events, and marine biodiversity loss. This exploratory study examines the association between residential proximity to the Mar Menor and childhood cancer incidence in Murcia from 2000 to 2018. In our case–control study of 594 cancer cases and 3564 controls, matched by birth year and sex, participants were categorized by proximity to the lagoon (G1 ≥ 20 km, G2 = 10–20 km, G3 = 2–10 km, G4 = ≤ 2 km). Odds ratios (ORs) and 95% confidence intervals (95%CI) were adjusted for sociodemographic and environmental covariates. Analysis of distance as a continuous variable indicated a decrease both in all types of cancer and lymphoid acute leukemia risk with greater distance (OR = 0.99; 95% CI 0.98–0.99), while as a categorical variable, it revealed a non-linear pattern. Specifically, the risk did not increase for those living within 2 km of the lagoon (OR = 0.87; 95% CI 0.52–1.37), whereas increased risks were observed in the 2–20 km range within Campo de Cartagena (G2; OR = 1.32; 95% CI 1.01–1.73 and G3; OR = 1.43; 95% CI 1.00–2.02). This suggests modulating factors near the lagoon may counterbalance risks from broader environmental contamination. These findings highlight the complexity of environmental health dynamics and the importance of detailed research to guide public health strategies and urban planning for environmental and child health protection.

Keywords Childhood cancer · Environmental health · Leukemia · Blue spaces · Epidemiology

1 Introduction

Blue spaces, encompassing natural water (rivers, lakes, and oceans) as well as urban aquatic (swimming pools and water parks) have garnered increasing attention in scientific research due to their impact on human health and well-being [1]. Green and blue spaces have been observed to have beneficial effects on both physical and mental health [2]. Specifically, there is

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emerging interest in whether exposure to blue spaces may be associated with a reduced risk of certain health outcomes [3], including childhood cancer incidence [4].

Over the last few years, the focus has been on the footprint that human beings can produce on the resources on which a large part of their economy is based and, therefore, on their survival. Among the most important resources for survival, one stands out above all, the water resource [5]. This resource has been affected over time by human-driven pressures from industrial development and agriculture. These activities have led to an increase in the levels of compounds such as nitrate, sulfides, and other elements, as well as chemical products, which have produced changes in water's composition, consequently arising in the ecosystems they house [6].

An example of this activity is the case of the Mar Menor Lagoon in the Region of Murcia, Spain. It is the Spanish lagoon with the largest extension of salt water in the Mediterranean Sea [7]. This coastal lagoon is regarded as one of the most ecologically rich ecosystems in the Mediterranean Basin [8]. Additionally, it is among the most significant environmental sites in the Mediterranean area, where many economic and industrial activities meet [9]. Its unique weather conditions and abundant natural resources have attracted tourism, recreational, and fishing uses, without forgetting the relevance of farming to the local economy [10].

Nevertheless, during the last decades, it has been seriously affected by the practice of intensive irrigation and the high pressure of construction in the area. This has led to an increase in nitrate levels in its waters [11], causing a process of eutrophication, affecting both its quality and the biodiversity it hosts [12, 13]. The situation, far from improving, has deteriorated [10]. The potential capacity for biological damage that this alteration can cause in the population near this lagoon is currently unknown. Due to its high ecosystemic values, this lagoon is under constant biomonitoring by the Spanish Institute of Oceanography (SIO), reporting its status periodically [14]. Children are among the most vulnerable to this phenomenon of contamination of its water.

A growing body of evidence suggests that exposure to natural environments, such as urban green space, may have a beneficial role in the prevention or survival of cancer, but the evidence is still inconclusive [15, 16]. But it is still more limited evidence regarding the effects of exposure to blue spaces and health [4].

Living near blue spaces like rivers, lakes, and oceans can have substantial health benefits, but the advantages may not extend to those who live farther away. Distance from blue spaces could lead to increased stress, lower physical activity, and less psychological well-being. Furthermore, proximity doesn't always equate to safety, as these areas are also often harbor pollutants from urban and agricultural runoff, posing health risks through exposure to contaminated water. Truly, the relationship is complex and not yet fully understood [17, 18]. These risks are particularly concerning for children who are more vulnerable to environmental toxins.

A child's development and growth stage are exposed to continuous changes during its process. Factors involved in this process include from genetic factors to environmental factors. Some of them have been described in the literature as risk factors for the appearance of oncological pathologies [19]. Among these pathologies, acute leukemia stands out, being the one with the highest incidence with a third of the tumors diagnosed in this stage of life, followed by lymphomas and tumors of the central nervous system [20].

Although childhood cancer is one of the leading causes of death in this population subset, to date, unfortunately, only approximately 10% of its etiology is known. Childhood cancer is closely linked to genetic alterations and prenatal exposures such as tobacco or alcohol consumption [21, 22]. Nevertheless, in recent years, attempts have been made to explore whether certain environmental factors such as agricultural land, industrial facilities, or home exposure to traffic may be related to an increased incidence of cancer [23–25]. Additionally, it is unknown if the contamination of water spaces, as is the case of the Mar Menor, can be a source of increased incidence. Therefore, this study aims to explore the possible relationship between the distance of exposure to this blue space and childhood cancer in the Region of Murcia.

2 Materials and methods

2.1 Study location

The Region of Murcia is a Mediterranean region located in the southeast of Spain (Fig. 1).

It has a population of approximately 1.5 million inhabitants spread over 45 municipalities, of which Murcia, Cartagena, Lorca, and Molina de Segura comprise more than 55% of the total population. There are currently 298,468 children under the age of 18 in the territory. The Region of Murcia is the second region with the lowest average income in Spain. The Mar Menor is a coastal lagoon in Murcia (South-East Spain), adjacent to the Campo de Cartagena area, where intensive

agricultural activity has taken place since the nineteen eighties. The total lagoon surface is 135 km², covers a coastline of 73 km, and contains five volcanic islands [10]. Moreover, it is considered a shallow lagoon, with an average depth of 4.4 m and being a maximum depth of around 7 m [10]. It is separated from the open sea by a 22-km-long sand bar (La Manga), although one natural inlet and two artificial channels allow some water renewal. The Campo de Cartagena occupies an area of 1609 km², of which the majority has discharged their runoff into the Mar Menor. There is a regular flux of groundwater, feeding these watercourses, and it receives agricultural runoff, treated urban effluents, runoff from old mining areas, and brackish water effluents. The Mar Menor becomes a bucket where heavy metals and organic chemical contaminants settle.

2.2 Sample selection

A population-based case–control study on childhood leukemia in the Region of Murcia, Spain, has been designed. The cases of this study have been provided by the Pediatric Environmental Health Unit (PESHU) of the Virgen de la Arrixaca University Clinical Hospital in Murcia. Murcia is a Mediterranean region in the southeast of Spain with a universal public health system that guarantees the treatment and follow-up of all children diagnosed with cancer. This regional centralized healthcare is in the Pediatric Oncohematology Section and the Pediatric Environmental Health Unit of the University Clinical Hospital of “Virgen de la Arrixaca” (Hospital Clínico Universitario Virgen de la Arrixaca) and facilitates access to almost 100% of the clinical history and professional contact with all children under 18 years of age with cancer and their families. The subjects of analysis were pediatric cancer cases diagnosed in the Region of Murcia (RM) between January 2000 and December 2018 by the MACAPEMUR (Environment and Pediatric Cancer in the Region of Murcia) project. MACAPEMUR is a project for the compilation of Pediatric Environmental History in newly diagnosed cancer patients since 1998 in this region. To avoid misclassifications or duplications, a doctor keeps an annual database log, and families are contacted in person or by phone. In addition, face-to-face interviews and follow-ups with the cancer patients and their caregivers are carried out by trained health professionals with experience in environmental and community health, pediatric oncology, and risk communication. Cases are classified according to the International Classification of Diseases for Oncology (ICD-O-3) and ICC-3 [26]. The project was approved by the ethics research committee of Clinical University Hospital Virgen de la Arrixaca [27]. The controls were extracted from the Birth Registry of the National Institute of Statistics (INE) [28]. Controls were randomly selected and matched to cases by geographic region to address according to municipality selection bias and enhance the study’s validity. Different stages were used for the geolocation process of the cases and controls. The georeferencing of the cases was carried out based on the address coordinates at the time of diagnosis. The georeferencing of the controls was carried out from the coordinates of the maternal address, provided by the National Institute of Statistics (INE) with a random error of 30 m to preserve anonymity. The coordinates of the cases were initially found in the cartographic reference system (CRS): EPSG 4326. Subsequently, they were re-projected to CRS: 25830, the system in which the controls were originally projected so that the data could be comparable under the same CRS. Then, a random sampling was performed, and controls were individually matched to cases by year of birth and sex in a 6:1 ratio. For the selection, sampling, and descriptive analysis processes, the QGIS and R® programs were used.

2.3 Measurement of exposure to the Mar Menor

After the geolocation of the cases and the controls selected for this study, we extracted the spatial polygon representing the Mar Menor from the cartographic bases of the National Institute of Geography (NIG). Subsequently, we have calculated the minimum distance in kilometers for each of the subjects to said space, and we have categorized said distance into five groups: G1 (reference) = ≥ 20 km, G2 = $> 10 - < 20$ km, G3 = $> 2 - \leq 10$ km, and G4 = ≤ 2 km (Fig. 2).

Fig. 1 Topographic map of the area selected for the study



2.4 Exposure to urban green and blue spaces

As covariates of the environment of the subjects of this study, we have calculated the exposure to urban green and blue spaces. We have used the available databases of the Information System on Land Occupation in Spain (SIOSE). This database, provided by the National Institute of Geography [23], divides the land into polygons of different sizes (0.5–2 ha). Each polygon is categorized by how much of its area is covered by different types of land cover. This classification is based on detailed geometric and thematic data, making it more accurate than using just satellite images. For this study, we decided to use the bases of 2005, 2011, and 2014.

After extracting the green and blue urban spaces from these cartographic bases, a buffer of 500 m distance from the subjects' homes was built. Then, we proceeded to dichotomize these variables (presence-absence of the green/blue space).

Furthermore, we used the previously created exposure buffer and assigned the mean value of the normalized difference vegetation index (NDVI) to each subject. This index is based on the combination of spectral bands recorded by satellites whose function is to enhance the vegetation based on its spectral response and attenuate the details of other elements, such as the ground. It is mainly used to estimate the quantity, quality, and development of the vegetation and to observe the variations of the vegetation cover throughout the seasonal periods. The value range of this index is from -1 to $+1$. The positive value is the one that represents the greenest surface [29]. We searched for the Landsat TM images with the lowest percentage of clouds and the highest possible NDVI value (spring–summer) for the same years as the SIOSES databases used (2005, 2011, and 2014). These images were extracted from the National Aeronautics and Space Administration's Earth Observing System Data and Information System [30].

2.5 Data analysis

Firstly, a descriptive analysis was carried out. This was divided into two parts: the first consists of a general descriptive analysis of the study subjects, and the second deals with the application of a statistical model of spatial point processes to evaluate the spatial distribution of the cases diagnosed each year and their relationship with the Mar Menor. The statistical model of spatial point processes measures and analyzes the intensity and behavior of an incidence of "x" event (in our study "tumors") creating a "heat map" of the incidence spatially.

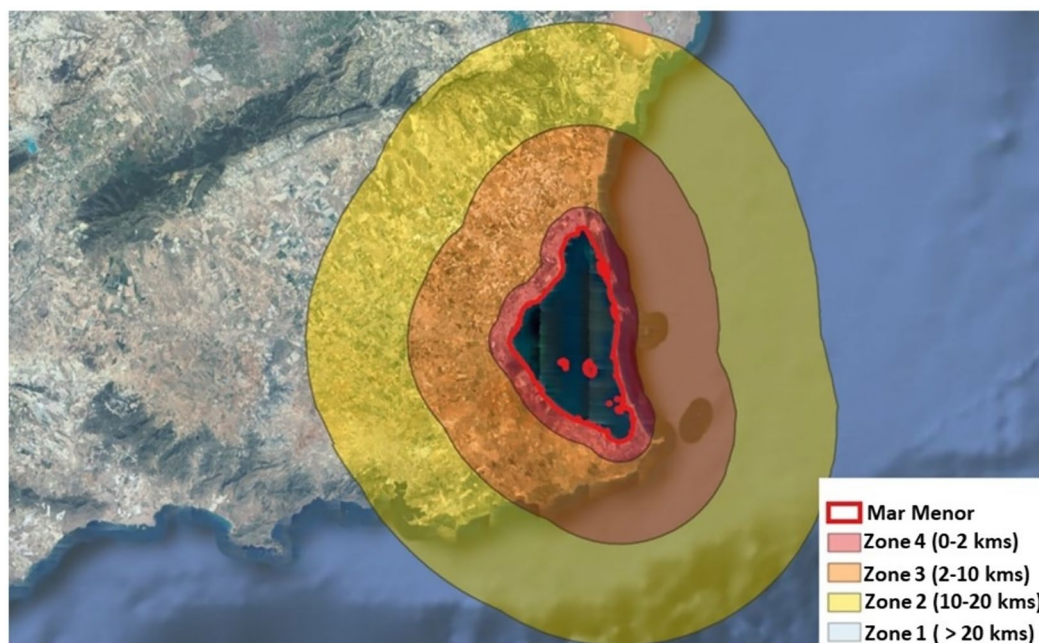


Fig. 2 Exposure zones were created around the perimeter of the Mar Menor

Secondly, the odds ratio and its 95% confidence interval (95%CI) was obtained to estimate the association between the distance to the Mar Menor and childhood cancer occurrence. To perform this, various unconditional multivariate logistic regression models were created where the variables sex, year of birth, exposure to urban green and blue spaces within a radius of 500 m, as well as the mean value of NDVI in said space were included in all of them for fitting the measurement association. The logistic regression model allows us to predict the likelihood that a subject belongs to one group or another (the response variable) based on predictor variables. Additionally, it helps us examine how one or more of these predictor variables are associated with the response variable, while accounting for the effects of other variables included in the model. To explore how this natural space could be linked with childhood cancer incidence, the distance to the sea was treated in the two previously explained ways: as a continuous variable and a categorized variable. In all the models, G1 was taken as the reference exposure group.

The statistical programs Microsoft Excel 2021®, R® version 4.1.1, STATA® version 16, and the geographic information system QGIS® version 3.18.2 were used. The tests conducted in this paper were found to be statistically significant if the p-value was less than 0.05.

3 Results

3.1 Descriptive analysis

The analysis included 594 cases and 3564 controls. Table 1 shows the characteristics of the children in the study. The main type of tumor diagnosed among all cases was childhood leukemia, which represented almost a third of the cases (30.5%), closely followed by tumors of the central nervous system (23.4%). The average age of diagnosis of the cases was around 5 years. Regarding the distance to the Mar Menor of the cases, the average was around 41 km, observing that the vast majority of them, 75.9%, were at a distance greater than 20 km.

In the initial leukemia analysis focusing on children diagnosed with childhood leukemia, there were no statistically significant differences when comparing their characteristics with the main group of cases. The leukemia group refers to cases of leukemia, which is the most common childhood cancer pathology and the one we have previously worked with in other studies due to its number of cases [4, 31]

We identified a third of the cases (33.83%) with the same address at birth and at the time of diagnosis. Their characteristics were not significantly different from those observed overall.

3.2 Analysis of specific processes

The analysis of a punctual pattern encompasses a series of techniques that allow us to study the distribution of a set of events. The interest in the use of these techniques arises in order to explore whether the diagnosed cases of any type of childhood tumor occurring in the Region of Murcia present an aggregation pattern or not.

Figure 3a and b illustrate the spatial distribution of all cases diagnosed yearly in the Region of Murcia. The main foci of cases diagnosed throughout all the years of the study occurred mainly in the municipalities near the coast and, therefore, the Mar Menor. Among these areas with a higher concentration of cases, the areas of the municipalities of Murcia and Cartagena stand out. A migration from the northwest/central areas to the Campo de Cartagena/Mar Menor is observed. Additionally, it can be seen that the years with the highest intensity occur from 2006 onwards.

3.3 Modelling of Mar Menor's effect

In our study, we focused on exploring how the distance variable could impact, as a continuous variable or categorized variable (taking G1 as the reference group) on the response variable (being case or not). The logistic regression model built was as follows:

$$(Y = k|X = x) = 11 + e - (\beta_0 + \beta_1 \text{Sex} + \beta_2(\text{Birth year}) + \beta_3 \text{Distance} + \beta_4 \text{NDVI} \\ + \beta_5(\text{Presence of green urban}) + \beta_6(\text{Presence of Blue Space}))$$

Table 1 Characteristics of cases, controls, and leukemia groups

Variables	Control (n = 3564)	Cases (n = 594)	Leukemia (n = 181)	p-value ^a	Same Address (n = 201)	p-value ^a
Sex						
Male	1914(53.7%)	319 (53.7%)	100 (55.2%)		105 (52.2%)	
Female	1650(46.3%)	275 (46.3%)	81 (44.8%)	0.715*	96 (47.8%)	0.719*
Age of Diagnostic media (DS)	–	5.1 (4.0)	5.2 (3.7)	0.843*	4.7 (4)	0.190 [#]
Type of tumor						
Leukemia	–	181 (30.5%)	–		50 (24.9%)	
CNS	–	139 (23.4%)	–		53 (26.4%)	
NBs	–	62 (10.4%)	–		27 (13.4%)	
Lymphomas	–	53 (8.9%)	–		19 (9.5%)	
Sarcomas	–	39 (6.6%)	–		16 (8.0%)	
Renal	–	33 (5.6%)	–		7 (3.5%)	
Other	–	92 (15.5%)	–	–	29 (14.4%)	0.262*
Presence of urban green spaces 500 m						
Yes	3439 (96.5%)	576 (97.0%)	173 (95.6%)		201 (100%)	
No	125 (3.5%)	18 (3.0%)	8 (4.4%)	0.363*	0	0.010*
Presence of blue spaces 500 m						
Yes	512 (14.4%)	76 (12.8%)	21 (11.6%)		22 (11.0%)	
No	3052 (85.6%)	518 (87.2%)	160 (88.4%)	0.671*	179 (89.0%)	0.491*
NDVI 500 m buffer, mediana (RIQ)	–0.05 (0.13)	–0.05 (0.15)	–0.04 (0.15)	0.669 [¥]	–0.06 (0.09)	0.012 [¥]
Distance from mar Menor (km)	45.6 (24.6)	41.0 (25.0)	40.6 (26.9)	0.864 [#]	40.2 (24.1)	0.678 [#]
Distance from mar Menor zones						
G1	2802(78.6%)	451 (75.9%)	134 (74.4%)		151 (75.1%)	
G2	397 (11.1%)	80 (13.5%)	24 (13.3%)		29 (14.4%)	
G3	192 (5.4%)	43 (7.3%)	14 (7.8%)		15 (7.5%)	
G4	155 (4.3%)	20 (3.4%)	8 (4.4%)	0.912*	6 (3.0%)	0.980*

CNS Central nervous system, NBs Neuroblastomas, G1 ≥ 20 kms; G2 zone = 10–20 kms; G3 = 2–10 kms; G4 (≤ 2 km)

^aP-value from main group of cases compared to leukemia group, [#]Student's t-test, [¥]Kruskal–Wallis test, *Chi-square test

Tables 2 and 3 show the ORs obtained for all the cases, and the cases diagnosed with lymphoid childhood acute leukemia. The estimates obtained in the models worked with the distance variable continuously (Table 2) show that, in any of the three groups of the analysis, the increase of one kilometer with respect to the Mar Menor leads to a decrease in the incidence of childhood tumors, being for cases of childhood leukemia this association greater (OR = 0.990; CI 95% 0.983–0.997).

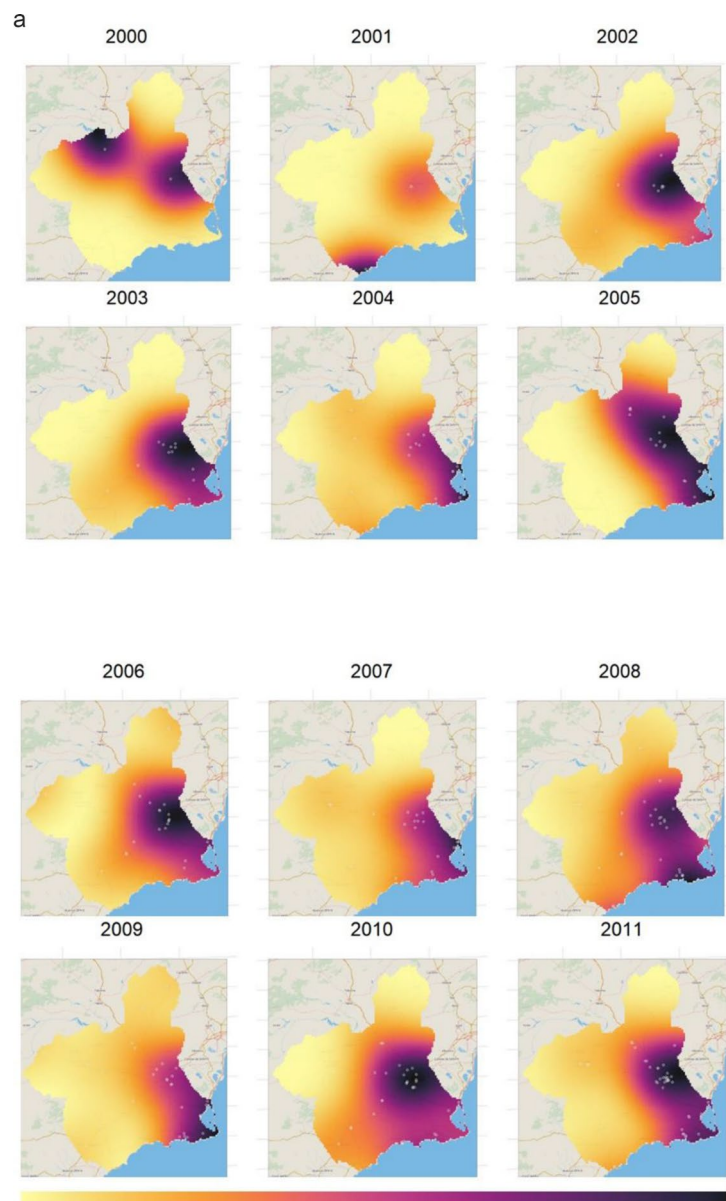
Regarding the comparative models (Table 3), we can observe how the incidence of childhood cancer is concentrated in the areas between 10 and 20 km (G2; OR = 1.32; 95% CI 1.01–1.73) and 2 to 10 km away from the Mar Menor (G3; OR = 1.43; 95% CI 1.00–2.02).

4 Discussion

In this study, we cautiously initiate a mapping of the influence of Mar Menor pollution on childhood cancer incidence in the Murcia region. Our findings tentatively indicate an association between childhood cancer and proximity to this particular blue space, requiring a careful interpretation due to the pioneering nature of the research area. The limited existing literature on the health effects of blue spaces [3, 4], is expanded upon by our methodology, which includes analysis of distance as both a continuous and a categorical variable. This approach revealed a decrease in cancer incidence with increased distance from the Mar Menor. However, the relationship is not linear when distance is categorized; notably, an increased risk is not apparent in the area closest to the sea (less than 2 km).

Particularly, areas G2 and G3, within Campo de Cartagena, showed higher incidence rates, reflecting the intense agricultural transformation and ecological costs of the region, a stark representation of environmental injustice. Yet,

Fig. 3 **a** Estimation of the intensity of childhood cancer cases diagnosed in the Region of Murcia, years 2000–2011. Lighter colors indicate low tumors incidences concentration while darkness colors indicate higher tumor concentration. **b** Estimation of the intensity of childhood cancer cases diagnosed in the Region of Murcia, years 2012–2018. Lighter colors indicate low tumors incidences concentration while darkness colors indicate higher tumor concentration



paradoxically, near-coastal areas (G4) indicate possible protective environmental factors against pollution. This complexity, intertwined with socio-economic disparities, underlines the multifaceted nature of health determinants [32, 33].

Murcia, Cartagena, La Manga, and San Javier, among others, are very close to the Mar Menor. These municipalities have grown in population in recent decades due to strong investment in construction and especially agriculture in the area. While the crude incidence rate across that entire period 1998–2020 in the Region of Murcia was 149.6 per 1 million, there was an increase over that time in the incidence. The areas with a higher standardized incidence ratio have shifted from the northwest (1998–2003) to the southeast (2016–2020) region [34].

Urbanization has been linked to increased risks of certain childhood cancers [35]. Our residual analysis from fitted models suggests a spatial distribution of cases that merits a deeper investigation into urbanization's role (Appendix A). Future research should include a detailed analysis of these spatial trends, taking into account that current studies have yet to fully explore all potential factors.

The direct and indirect consequences of Mar Menor's pollution are critical, with areas G2 and G3 within Campo de Cartagena, characterized by intense agricultural industrialization, and presenting the highest childhood cancer rates. This region's ecological decline due to intensive agriculture has resulted in significant environmental costs, contributing to poverty and social exclusion, the highest being in Campo de Cartagena/Mar Menor [32]. This environmental degradation

Fig. 3 (continued)

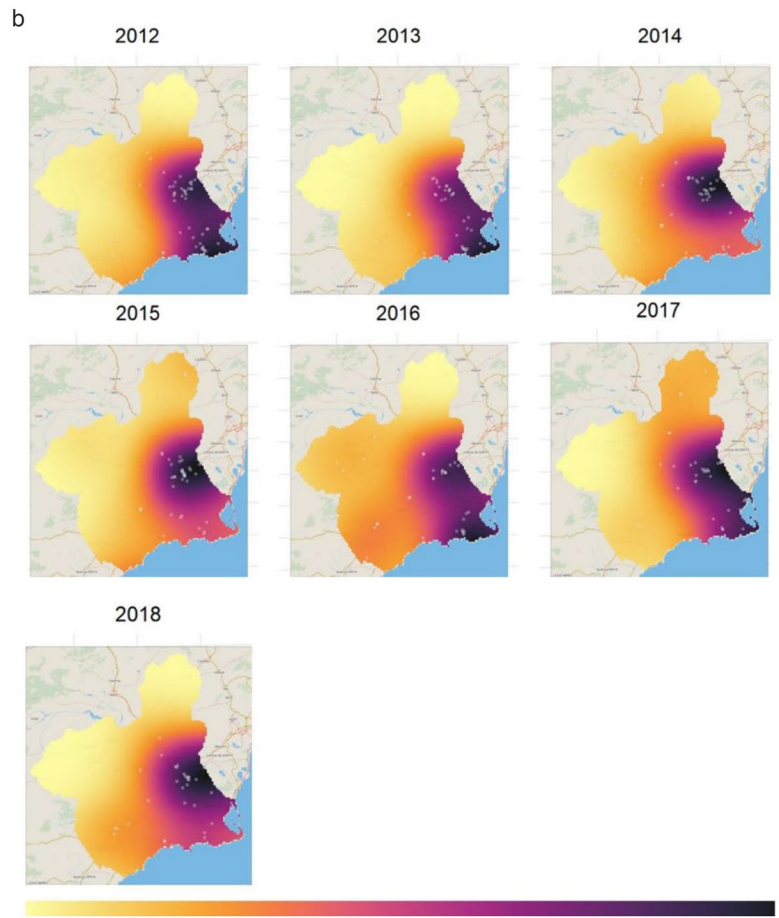


Table 2 Analysis of the distance to the Mar Menor as a continuous variable

Distance from Mar Menor	All type of cancer	Lymphoid acute leukemia	Same address (all types of cancer)
Simple model OR (CI 95%)	0.99 (0.98–0.99)	0.99 (0.984–0.99)	0.99 (0.98–0.99)
Adjusted model OR (CI 95%)	0.99 (0.98–0.99)	0.99 (0.98–0.99)	0.98 (0.98–0.99)

Simple models and models adjusted for sex, date of birth and covariates of exposure to urban green and blue spaces in a buffer of 500 m for the group of childhood tumors, childhood leukemias and subjects with unchanged address

CI Confidence Interval

has exacerbated flooding and pollution in Mar Menor, leading to biodiversity loss and anoxia [33, 36], and illustrating a cycle of poverty-induced environmental damage [37], highlighting a clear case of environmental injustice.

Legislative responses to this injustice include the Mar Menor laws, targeting ecological restoration in the affected areas [33]. Community advocacy, notably from children, has been instrumental in these changes, culminating in Law 19/2022, which declares Mar Menor a ‘legal person’—a landmark for European environmental law [38], aligning with international trends in granting legal rights to natural entities, such as in Ecuador, Colombia, India, and New Zealand’s recognition of the Whanganui River.

For decades, the Mar Menor Lagoon has been significantly impacted by anthropogenic activities, with its current compromised state being a cumulative consequence of various mining, intensive agriculture, and industrial processes. These activities have precipitated a fundamental shift in the lagoon’s ecological balance [9]. Research has increasingly demonstrated the connection between water pollution and the rise of oncological diseases, implicating the toxicological

Table 3 Analysis of the distance to the Mar Menor as a categorized variable

Distance from mar Menor	All cases	Lymphoid acute leukemia	Same address (all types of cancer)
Simple Model OR (CI 95%)			
G1 (reference)			
G2 (10–20 kms)	1.22 (0.95–1.59)	1.26 (0.79–1.94)	1.33 (0.86–1.97)
G3 (2–10 kms)	1.35 (0.95–1.89)	1.42 (0.77–2.44)	1.41 (0.78–2.36)
G4 (≤ 2 km)	0.78 (0.47–1.23)	1.04 (0.46–2.04)	0.70 (0.27–1.47)
Adjusted Model OR (CI 95%)			
G1 (reference)			
G2 (10–20 kms)	1.32 (1.01–1.73)*	1.29 (0.80–2.03)	1.35 (0.86–2.04)
G3 (2–10 kms)	1.43 (1.00–2.02)*	1.52 (0.81–2.65)	1.43 (0.79–2.45)
G4 (≤ 2 km)	0.87 (0.52–1.37)	1.15 (0.50–2.27)	0.70 (0.27–1.48)

Simple models and models adjusted for sex, date of birth and covariates of exposure to urban green and blue spaces in a buffer of 500 m for the group of childhood tumors, childhood leukemias and subjects with unchanged address

G1 = reference group (subjects at a distance greater than or equal to 20 km from the Mar Menor)

*The results are statistically significant with $p < 0.05$. CI confidence interval

effects of waterborne contaminants on human genetics [39–41]. In addition, some of its possible indirect impacts on health could be related to recreational activities in its surroundings, leading to greater sun exposure and an increased risk of skin cancer [42]. Our study sets a precedent for other blue spaces facing similar challenges, protecting and promoting both Nature and Child rights. Significantly, the Act on Guardians of Mar Menor must recognize and empower the vital role of children, whose natural and innate, and often passionate, interest that children show in preserving the environment makes them a dynamic and powerful force in protecting the Mar Menor.

On the other hand, blue spaces like the Mar Menor could potentially mitigate the effects of pollution in terrestrial areas, serving as a protective component [43]. There is growing evidence that spending time in or around water bodies or 'blue spaces' can lead to improved human health [17, 44–46]. In particular, the sea breeze and marine environment have been shown to enhance air quality by dispersing pollutants, thereby reducing exposure for coastal populations [43]. Given these potential benefits, safeguarding blue spaces like the Mar Menor is essential for global health initiatives, particularly when aiming to reduce the impacts of pollution on children, one of the most vulnerable groups.

Regarding childhood cancer, there hasn't been research linking it to water pollution. To adequately determine the presence of toxic metabolites or not in children, exhaustive monitoring of them would be necessary, which entails a high cost. However, other environmental factors have been related to an increase in the incidence of childhood cancer, such as exposure to pesticides, industries, or exposure to traffic. All of them without being able to analytically objectify toxic compounds in organisms or even clarify a plausible etiopathogenic mechanism [23, 25, 47].

Likewise, other factors, such as those related to the environment and the parents' habits, also play a fundamental role in the appearance of childhood cancer during the initial phases of children's development. Among them, we can highlight how the consumption of drugs, tobacco, or parental exposure to industries or tobacco during pregnancy has been related to the appearance of childhood cancer [48–51]. To date, these exposures are more complex to measure because a national collection system for children's habits and immediate environment has not been developed. However, this collection of such specific information has begun to be developed by the Pediatric Environmental Health Units [52]. For future studies, this could have a very important value when investigating other environmental factors possibly related to childhood cancer.

However, environmental factors have recently been studied and could reduce childhood cancer incidence, particularly in urban green spaces and blue spaces. After having developed a methodology that has allowed us to explore these spaces, we decided to apply it in this study [4]. To date, there is no consensus on the possible optimal distances to measure the effects of these spaces [53, 54], so, based on our previous results, we decided to use an exposure buffer of 500 m.

Regarding the specific groups, cases diagnosed with childhood leukemia, and cases whose address was the same at birth and diagnosed time, their characteristics and the results obtained from the logistic regression models do not

present significant differences with the general group of cases. This could be explained by these subgroups' great weight concerning the general set of cases. However, for future studies, it would be interesting to break down the characteristics of the rest of the tumor types and/or determine other possible sensitivity groups, such as those children whose age at the time of diagnosis is less than 12 months.

The limitations of this work are typical of a case–control study, including potential biases in the identification of cases and controls, the inability to calculate incidence or relative risk, as well as the difficulty in establishing causality and temporality. Additionally, there are inherent limitations of the study, such as the absence of individual-level data, the possible measurement error between the maternal address at birth and the direction at the time of diagnosis, the lack of socioeconomic variables and the exclusion of various environmental variables from our models. However, we believe that this work establishes an interesting knowledge base that could open new avenues of research in this field and contribute to improving the health and quality of life of children.

5 Conclusion

To the best of our understanding, this investigation represents the inaugural effort to elucidate the connection between the Mar Menor Lagoon, a significant blue space, and the incidence of childhood cancer. Our findings preliminarily suggest a relationship, indicated by a lower incidence of cancer with increasing distance from this natural habitat. Interestingly, blue spaces might also serve as buffers to the adverse health outcomes associated with environmental pollutants in nearby agricultural and urban coastal areas. However, due to substantial limitations—such as the absence of individual-level subject data and the exclusion of various environmental variables from our models—our conclusions must be drawn with prudence. Further research is essential to deepen our comprehension of these associations. The insights gained hold the potential to inform urban and public health planning substantially, facilitating the development of strategies that protect both the environment and the welfare of children.

Author contributions Conceptualization: COS and JAOG; data curation: COS; formal analysis: COS; funding acquisition: JAOG and RRP; investigation: COS; methodology: COS, JAOG, RRP and GFA; project administration: RRP and GFA; resources: JAOG and RRP; software: COS; supervision: RRP and GFA; validation: RRP, JAOG and GFA; visualization: COS; roles/writing—original draft: COS and JAOG; writing—review & editing: JAOG, GFA, RRP, EOP.

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Availability of data and materials The datasets generated during and/or analyzed in the current study are not publicly available due to the fact that the geographical coordinates of the study subjects are considered private information. These coordinates are subject to privacy restrictions. Therefore, it is not possible to publicly share the data containing this confidential information. However, the data are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate The MACAPEMUR (Environment and Pediatric Cancer in the RM) project was approved by the ethics research committee of Clinical University Hospital Virgen de la Arrixaca. Informed consent forms signed by all parents and children over 12 were collected. The study was performed in accordance with relevant guidelines and regulations as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Competing interests The authors declare that they have no competing interests.

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