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Association of airborne toxins with geographic clustering of cutaneous T-cell lymphoma in Louisiana

Jalal Maghfour
Henry Ford Health, jmaghfo1@hfhs.org

Frances Gill

Justin Olson

Nicholas Guido

Harika Echuri

See next page for additional authors

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Authors
Jalal Maghfour, Frances Gill, Justin Olson, Nicholas Guido, Harika Echuri, and Andrea Murina

Research letter

Association of airborne toxins with geographic clustering of cutaneous T-cell lymphoma in Louisiana

To the Editor: Cutaneous T-cell lymphoma (CTCL) incidence has increased over the past decade.[1] Recent studies have alluded to the role of environmental factors, particularly benzene and trichloroethylene (TCE), in disease development.[1] We sought to examine whether CTCL clustering exists in the state of Louisiana and assess the relationship of the clusters with benzene and TCE exposure. The statewide county-level incidence and demographics were derived from the Louisiana Tumor Registry, which includes patients with CTCL from 2000 to 2018. Histology codes were derived from the *International Classification of Diseases for Oncology* codes.[2] Exposure concentrations of benzene and TCE between 1996 and 2011 were collected from the Environmental Protection Agency's National Air Toxics Assessment database. Geographical clustering of CTCL was performed using the local Moran I statistic.

Seven hundred and seventy-four patients with CTCL (415 [53.6%] women, 496 [64.8%] Whites) were

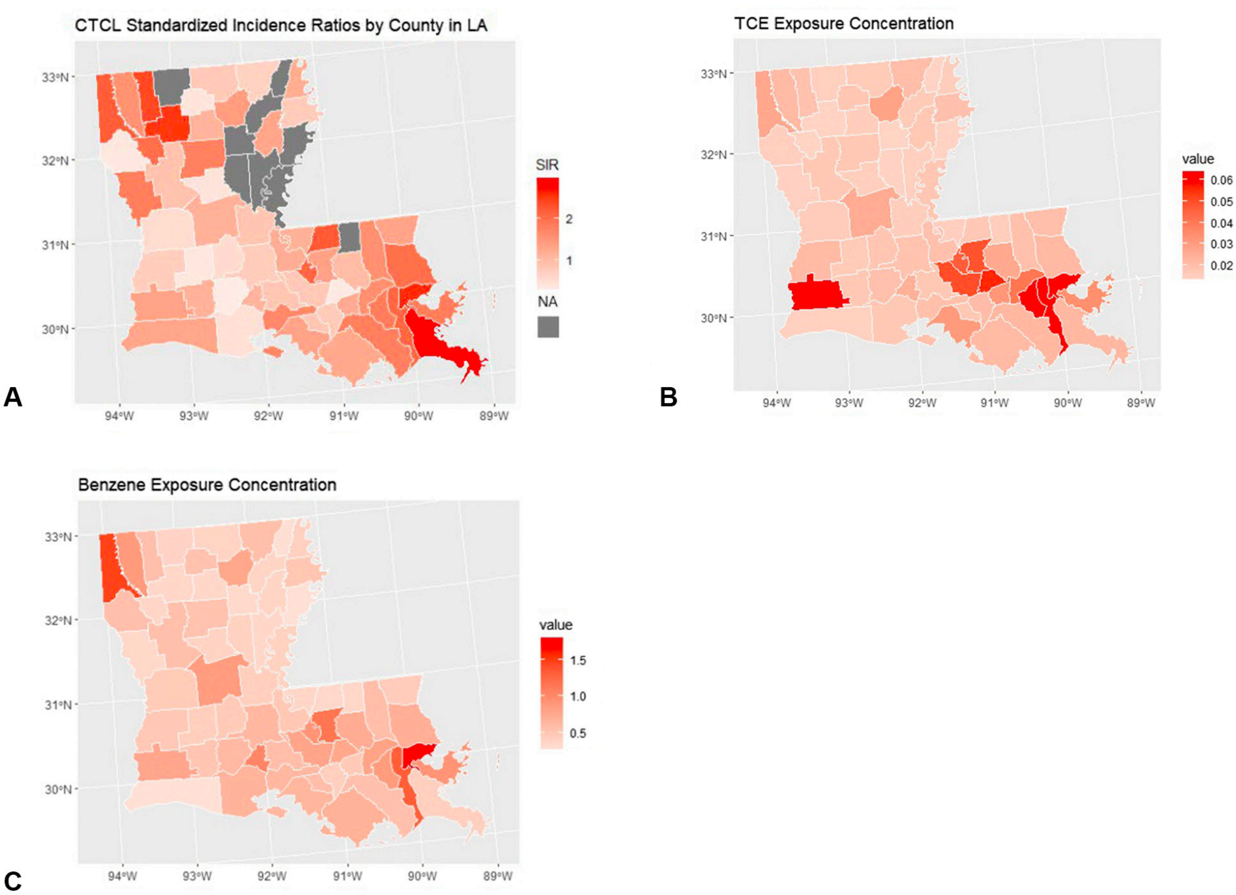

Fig 1. A, Spatial distribution of cutaneous T-cell lymphoma (CTCL) incidence as standardized incidence ratio; NA refers to counties with an estimated population of less than 10,000 individuals and those without any reported CTCL cases; (**B**) Spatial distribution of trichloroethylene (TCE) with a degree of exposure represented in $\mu g/m^3$ unit; the various shades of *red* represent the relative amount of exposure to concentrations of TCE in each county. Higher TCE exposure is illustrated as *bright red*, while low toxin exposure is depicted as *faint red* to *pink color*. (**C**) Spatial distribution of benzene with a degree of exposure is represented in $\mu g/m^3$ unit; the various shades of *red* represent the relative amount of exposure to concentrations of benzene in each county. Higher benzene exposure is illustrated as *bright red*, while low benzene exposure is depicted as *faint red* to *pink color*.

identified; the mean standardized incidence ratio was 1.24 (Fig 1). The link between TCE/benzene exposure concentrations, the median income (a surrogate for socioeconomic status), and CTCL was assessed using multivariate spatial analysis, in which neighborhood effect was included as an independent variable. Of note, a neighborhood effect is the independent causal effect of a neighborhood (eg, residential community) on any number of health and/or social outcome.

Median income ($P = .92$), TCE exposure ($P = .98$), and benzene exposure ($P = .12$) were not associated with CTCL incidence. The spatial dependence effect included in this model was significant ($\rho = 0.42$, $P = .004$), indicating a 42% correlation between the incidence in an observed county and the average incidence of its neighbors.

We identified 2 significant "high-high" cluster areas of high incidence surrounded by other areas of high incidence (Fig 2). This aligns with the results obtained from multivariate spatial analysis, which suggest a spatial effect. We also detected a cluster containing significantly low levels of CTCL incidence (Fig 2). In this low cluster, the average benzene and TCE exposures were 0.24 and 0.010 $\mu g/m^3$, respectively; these levels were lower than the local state levels (average benzene exposure: 0.32 $\mu g/m^3$, average TCE exposure: 0.017 $\mu g/m^3$).

The results of our study demonstrated the nonrandom clustering of CTCL and the significant impact of neighborhood effects on CTCL incidence. These findings are consistent with those of previous studies supporting CTCL clustering at national and global levels.[3,4] Neighborhood effects on CTCL clustering strongly suggests that extrinsic factors may play a role in its development. While there was not a significant effect of TCE and benzene on CTCL incidence, the multicounty cluster of "high-high" incidence results surrounding New Orleans (Fig 2) also includes the counties with some of the highest benzene- and TCE- exposure levels observed in Louisiana.

Some of the limitations include the potential misclassification of CTCL as a peripheral T-cell lymphoma. Additionally, we were unable to account for the duration of exposure or the many pathways of human exposure. Occupational exposure could contribute to benzene and TCE exposure, but this was not recorded.

CTCL exhibited a nonrandom geographic clustering with a neighborhood effect that influences disease incidence. These findings highlight the need for additional studies exploring the factors that contribute to CTCL clustering.

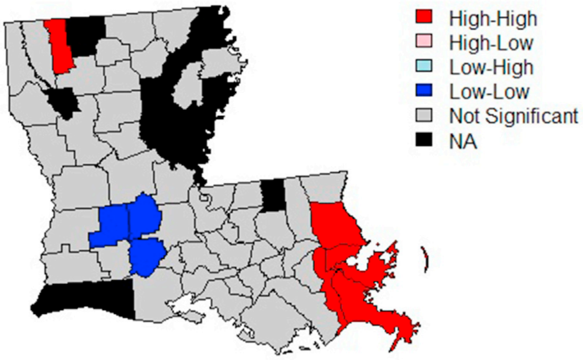

Fig 2. Local Moran I statistic results are illustrated for Louisiana County. *Dark red* indicates "high-high" areas (areas of high values surrounded by other areas of high values); *Blue* indicates "low-low." NA refers to counties with a population of <10,000 people and also included counties without any reported cutaneous T-cell lymphoma cases.

Jalal Maghfour, MD,[a] Frances Gill, MD, MPH,[b] Justin Olson, BS,[c] Nicholas Guido, MD,[d] Harika Echuri, BS,[e] and Andrea Murina, MD[e]

From the Department of Dermatology, Henry Ford Hospital, Detroit, Michigan,[a] the Department of Psychiatry, University of Southern-California, Los Angeles, California,[b] Data Science, Ashley Furniture, Arcadia, Wisconsin,[c] Private Practice, Dermatology LTD, Media, Pennsylvania,[d] and the Department of Dermatology, Tulane University, New Orleans, Louisiana.[e]

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Key words: benzene; CTCL; cutaneous T-cell lymphoma; carcinogen; environmental exposure; geographic clustering; incidence; mycosis fungoides; neighborhood effects; trichloroethylene; T cell.

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Correspondence to: Andrea Murina, MD, Associate Professor of Dermatology, Dermatology Department, Tulane University School of Medicine, 1430 Tulane Avenue, Suite 8036, New Orleans, LA 70112

E-mail: amurina@tulane.edu

Conflicts of interest

Dr Murina is a speaker for AbbVie, Amgen, Eli Lilly and Company, Janssen, Ortho-Dermatologics and a consultant for Janssen, Novartis, and UCB.

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