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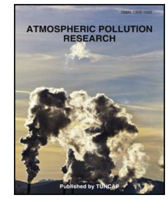

Thyroid cancer incidence in women and proximity to industrial air pollution sources: A spatial analysis in a middle size city in Colombia

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ABSTRACT

Manizales, a mid-size city in Colombia, hosts industries like metallurgy, electrical, chemical, and rubber and plastic industrial facilities that have released into atmosphere some pollutants postulated as thyroid cancer (TC) promoters, such as dioxins and furans, dichloromethane, lead and copper. In this article we aim to detect clusters of TC and analyze their spatial association with industrial pollution. TC cases (2003–2010) were obtained from Manizales' Population-based Cancer Registry (PCR-Mz). Atmospheric emissions from industries were obtained from official reports of environmental authority. Data was spatially aggregated into census tracts and analyzed with Bayesian Besag-York and Mollié (BYM) models. Three exposure approaches were used: i) presence or absence of industries into census tracts, ii) sum of air discharges, and iii) an exposure index (EI) that considered the distance and orientation of the census tract regard to industries, average wind direction and speed, and population mobility. Models were fitted by exposure definition and sex, and included traffic and socioeconomic variables for adjustment. Using the Kulldorff's spatial exploration statistic we also performed point-data analyses in order to detect and localize clusters with individual data.

Ecological regression models showed that, for women, smoothed standardized incidence ratio (sSIR) increase in 15% [95% credibility interval: 3–27%] and 63% [95%CI: 18–125%] per one standard deviation increase in EI for dichloromethane and PCDDs/Fs, respectively. Point-data analysis confirmed a cluster of female cases close to an industry emitting chlorinated solvents. These results suggest that dichloromethane and PCDDs/Fs emitted from industrial sources might be suspected as thyroid cancer risk factors.

1. Introduction

Manizales is a city localized in a high altitude valley (2150 m.a.s.l) in the Andean region of Colombia, South America, with about 400,000 mostly (93%) urban inhabitants (DANE, 2005). It has a tradition of industrial activities, spanning several decades, with main activities being metallurgy and metal processing, manufacture of electrical appliances, chemical industry, rubber and plastic, food products and other manufactures (Soto-Vallejo et al., 2009). Local researchers have warned against the risks of air pollution in Manizales due to the high presence of industrial sources besides its topography, meteorology, traffic emissions and population crowding in urban zones (Aristizábal et al., 2011). In a recent paper, we identified 36 industrial facilities in Manizales that have emitted air pollutants such as metals, polychlorinated dioxins and furans, and chlorinated solvents, which have been pointed out like potential thyroid carcinogens. Atmospheric emissions from several industries have exceeded regulatory limits, including those of potential carcinogens (Arias-Ortiz and Ruiz-Rudolph, 2017).

In this context, health surveillance became critical, and one outcome that has shown unusually high rates in Manizales is thyroid cancer, with rates much higher than other cities in Colombia and South America. Age-standardized incidence rates (ASIR) for 2003–2007 were 12.4 per 100,000 person-year for women and 3.7 for men (López-Guarnizo et al., 2012), while in other Colombian cities -Bucaramanga, Cali and Pasto-the ASIRs were 9.6, 11.3, y 8.4 for women and 2.6, 2.3 y 2.4 for men, respectively (Bravo et al., 2012; Uribe et al., 2012; Yépez et al., 2012). Worldwide, Manizales is in the top 50 of cities with population-based cancer registries (IARC et al., 2014). Incidence

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Abbreviations

ASIR	age-standardized incidence rates
m.a.s.l	meters above sea level
BYM	Besag, York and Mollié Bayesian models
sSIR	smoothed standardized incidence ratio
US-EPA	United States Environmental Protection Agency
EDC	endocrine disruptor chemical
HHT	hypothalamic-hypophysis-thyroid axis
PCB	polychlorinated byphenyls
PBDE	polybrominated byphenyls
DANE	National Department of Statistics, by its Spanish acronym
CAR	convolution auto-regressive distribution
PCR-Mz	Population-based Cancer Registry of Manizales
PP	posterior probability from BYM model
RFs	reporting facilities, or industrial facilities required to report atmospheric emissions of specific pollutants
Non-RFs	non-reporting facilities, or industrial facilities not required to report atmospheric emissions of specific pollutants but belonging to the same standard industrial classification (SIC) that RFs
PCDDs/Fs	poly-chlorinated dibenzo-dioxins and furans
LCI	living-conditions index
MPL	maximum permitted limits

estimations for 2008–2012 are even higher, with ASIR of 23.2 y 4.6 per 100.000 in women and men, respectively (Bray et al., 2017).

Despite a marked worldwide increase in thyroid cancer incidence in recent decades (Pellegriti et al., 2013), few risk factors have been demonstrated (Meinhold et al., 2010), being ionizing radiation the only one confirmed (Brown et al., 2012; Hard, 1998). Iodine intake deficiency has been only associated with follicular carcinoma (Pellegriti et al., 2013), but it is a less relevant risk factor because many countries, including Colombia, are adding iodine to salt for human consumption.

Some environmental risk factors for thyroid cancer have been proposed, including intake of nitrates in food and water (Ward et al., 2010), and occupational exposure to industrial solvents, formaldehyde and pesticides (WHO-UNEP, 2013). Pesticides have been shown to induce tumors in rodents follicular cells by non-mutagenic mechanisms (Hurley, 1998), or showed inhibitory activity on thyroid peroxidase, increased hepatic metabolism and excretion of thyroid hormones (WHO-UNEP, 2013). Several chemicals have been postulated as endocrine disruptors (EDCs) of the hypothalamic-hypophysis-thyroid (HHT) axis (WHO-UNEP, 2013). Evidences have been observed for phthalates, PCB and PBDEs both in animals and humans (Baccarelli et al., 2008; Chevrier et al., 2007; Hombach-Klonisch et al., 2013; Meeker et al., 2007; Shen et al., 2011; Zhang et al., 2009). However, evidence of these mechanism as risk factor of thyroid cancer in human populations remains unclear (Aschebrook-Kilfoy et al., 2015, 2014; WHO-UNEP, 2013).

In this context Manizales presents many opportunities to study the impacts of industrial pollution on thyroid cancer. First, industrial facilities have been present close or within urban areas for decades, with many of them releasing suspected thyroid carcinogens postulated by Leux and Guénel (2010); second, the high thyroid cancer incidence reported suggests a major risk factor affecting the city; and third, the existence of a population-based cancer registry with high quality data.

The aim of this study is to detect clusters of thyroid cancer using spatial analysis of aggregated data (smoothed standardized incidence ratio at census tracts) and point data (individual cases location), and assess whether the clusters are associated with industrial sources of specific air pollutants.

2. Methods

2.1. Study design

We performed a spatial analysis combining two approaches. First, an ecological small-area incidence study, using census tracts as the unit of analysis, in order to determine tracts with unusually high incidence rates and estimate associations between industrial sources of air pollutants and thyroid cancer. Second, we performed a point-data analysis, in order to detect and locate spatial clusters of thyroid cancer cases. Both methodological approaches have been widely used and have important developments in the last two decades (Beale et al., 2008; Elliott and Wartenberg, 2004; Lawson et al., 1999; Lertxundi-Manterola, 2006; Santamaría-Ulloa, 2003). We adopt these two approaches because they are considered the first step in the exploration and verification of hypotheses in the ecological level, which serve as a justification for more complex and costly later studies.

We focused on industrial facilities that were more likely to affect thyroid cancer incidence, and thus were selected following these criteria: i) facilities located in urban Manizales, as they are more likely to produce higher exposures in the population; ii) those operating before 1994, considering likely latency periods for thyroid cancer (Hallquist et al., 1993; Ron et al., 1995); and iii) industrial facilities reporting air emissions of suspected thyroid carcinogens like polychlorinated dioxins and furans (PCDDs/DFs) (Pesatori et al., 2009), metals such as cadmium, copper, lead, mercury, nickel, or zinc (Kouniavsky and Zeiger, 2010; Leux and Guénel, 2010; Vigneri et al., 2015), and chlorinated solvents (Barragán-Martínez et al., 2012; Benvenga et al., 2015; Lope et al., 2005; Wingren et al., 1995; Wong et al., 2006).

2.2. Industrial facilities

We performed an exhaustive search of industrial facilities in the urban area of Manizales, geo-referenced them, and characterized their emissions. Industrial facilities were identified from environment official records and from enterprise census. In order to estimate the atmospheric discharges of pollutants two approaches were followed, depending on whether facilities were required to report air pollutants. In the first, industries required to state air pollution releases – reporting facilities (RFs)– were identified using official records, and data about emissions of specific pollutants were extracted; also, a per-employee emission rate was calculated for each pollutant. Detailed information about kind of contaminants, methods and years of available data in official records can be found in Supplementary Table 1. In the second approach, industrial facilities not required to state air pollution releases – non-reporting facilities (non-RFs)–, but belonging to the same Standard Industrial Classification codes than the RFs, were also identified from enterprise census. According to current legislation, these industries are exempt from reporting air emissions primarily by its size, as most of them are micro and small businesses, but including them is critical because they are companies with less infrastructure and capacity to implement clean technologies, and some of them are still using quasi-artisanal methods that might be more polluting. Emissions of specific pollutants from non-FRs were calculated based on the number of employees and the per-employee rates calculated previously (Dolinoy and Miranda, 2004). Initially, we identify 36 industrial facilities that have emitted PCDDs/DFs, lead, copper, and dichloromethane (Arias-Ortiz and Ruiz-Rudolph, 2017). After applying selection criteria described in section 2.1 (only industries located in urban zone that started operations before 1994), only 28 industries met the selection criteria. Geographical coordinates and addresses were obtained for each facility and geo-referenced using the Google© Street View tool.