

Cod: 8.1008

PREVALENCE OF DIABETES MELLITUS IN THE SEVESO, ITALY COHORT 2006-2014

L. Cavalieri D'oro¹, M. Rognoni¹, D. Consonni², A.C. Pesatori³, P.A. Bertazzi²

¹*Epidemiology Unit – Cancer Registry, Agency for Health Protection (ATS) of Brianza, Monza, Italy*

²*Epidemiology Unit, Department of Preventive Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*

³*Epidemiology Unit, Department of Preventive Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy*

Introduction

The Seveso, Italy, dioxin episode caused severe 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure to a population comprising people of both genders and all ages, with little or no interference by other contaminants. The accident took place on July 10, 1976, in the trichlorophenol production department of a chemical plant located near the town of Seveso, 25 km north of Milan. A chemical cloud containing several kilograms of TCDD was released into the environment and contaminated a vast and densely populated area.

Three zones with decreasing soil TCDD levels were delimited: A (highest), B (high) and R (low). The cohort of residents in the contaminated zones and in a surrounding non-contaminated (non-ABR) referent area has been followed-up for mortality and cancer incidence since 1976. Subjects were assigned to one of the zones (A, B, R, or reference) based on their official residence on the day of the accident. Residence has the advantage of being highly reliable and readily available for every member of this large cohort; in the Lombardy region of Italy, it is highly concordant with actual domicile (>95%). Several studies showed that TCDD blood levels of TCDD in samples of subjects were highly associated with residence, while other congeners (PCDD, PCDF, and PCB) did not show differences across zones (Consonni et al. 2012).

A relationship between TCDD and diabetes mellitus has been postulated based on animal and epidemiological studies, including ours (a DM mortality increase in zone B women as of 2001) (Consonni et al. 2008).

Since 2005 the Lombardy Region implemented an integrated system (Banca Dati Assisititi, BDA) to identify subjects with selected chronic diseases by exploiting several data sources (e.g. hospital inpatient discharge records; drug prescription; exemption from payment).

In preliminary 2006-2008 analysis, we found a prevalence excess of DM among Zone B residents compared with non-ABR (40% in women and 28% in men); data for 2006-2011 confirmed the excesses (21% women and 23% in men) (Cavalieri d'Oro et al. 2013).

Materials and methods

BDA is a classification system of the population that has been developed in Lombardy on the basis of criteria identified by technical working groups using sets of rules to classify at an individual level resident people as affected by selected groups of chronic diseases (e.g. malignant neoplasms, diabetes, heart diseases, neurologic? diseases, autoimmune diseases, endocrine diseases, etc.) and to evaluate their costs.

For instance, BDA is useful for planning and monitoring of health policies: it can be used to estimate the prevalence of chronic degenerative diseases, their spatial distribution and their evolution in time; to estimate per-capita and total expenditure for each disease or combination of diseases, to evaluate disaggregated consumption for categories of disease, gender, age group, geographical area.

Using unique personal identifiers (fiscal code), we performed a deterministic record-linkage between residents on the day of the accident alive on January 1st, 2006 and the local BDA database (years 2006-2014, 850.000 people covered). Prevalent cases of DM were identified as follows: hospital inpatients discharged with Diagnostic Related Group (DRG) 294 or 295, or with code 250.xx of the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) in any diagnosis position; use of drugs identified in the Anatomic Therapeutic Chemical (ATC) Classification

System with codes A10A (insulin >10% yearly Defined Daily Dose - DDD) or A10B (oral antidiabetic >30% yearly DDD); payment exemption code 013x (Diabetes Mellitus).

Prevalence of Diabetes Mellitus was calculated for residents in each zone on the basis of the official residence on the day of the accident and alive on 01.01.2006. The cohort was followed-up for obtaining the vital status.

We used logistic regression controlling for gender and age to calculate prevalence odds ratios (OR) and 95% confidence intervals (CI). We performed further analyses using logistic regression models adjusted for gender, age and those comorbidities that could be read as proxy of body mass index in the BDA system (hypercholesterolemia, hypertension, cardiovascular diseases). Deterministic record linkage between the Seveso cohort and BDA was performed using SAS Software, version 9.2, and statistical analysis was performed using Stata Software, version 13.

Results and discussion:

The mean percentage of cohort subjects linked to BDA was 78.7%, ranging from 80.7% to 82.4% in the three polluted zones (Table 1). Mean prevalence of DM was 10.1% and ranged across zones from 9.5 to 11.3%.

We confirmed among both genders previous finding of increased diabetes mellitus prevalence in zone B: among men we found 205 cases (OR=1.31, 95% CI 1.12-1.53), and among women 152 cases (OR 1.17, 95% CI 0.98-1.39). These results were confirmed even after adjusting for surrogate markers for body mass index (arterial hypertension, cardiovascular diseases, hypercholesterolemia). No increased prevalence was found in zone A, while only a modest excess was found in females in zone R (Table 2). A point that can be underlined is the time evolution of evidences of prevalence in Zone B (Figure 1): prevalence OR among females in the period 2006-2008 was higher as compared with males, the point estimate was nearly identical for both genders in the period 2006-2011 and the prevalence OR for males was higher than the prevalence OR for females in 2006-2014.

This analysis adds some evidence in favour of the association between TCDD exposure and Diabetes Mellitus occurrence (stronger among males). The following limitations must be taken into account: BDA does not cover people who emigrated outside the province of Monza and Brianza; BDA is only available for recent years, therefore only cohort survivors 30 years after the accident could be studied; we had proxy information on some confounders; no increased risk was found in the most polluted zone A.

Acknowledgements:

The authors acknowledge the Health Directorate, Lombardy region for supporting local Epidemiology Units and the Directors of Local Health Authority for their trust in the Epidemiology Unit of Brianza.

References:

1. Consonni, D, Sindaco, R., Agnello, L., Caporaso, N. E., Landi, M. T., Pesatori, A. C., and Bertazzi, P. A. (2012) *Med Lav* 103(4):259-267
2. Consonni, D., Pesatori, A. C., Zocchetti, C., Sindaco, R., Cavalieri D'Oro, L., Rubagotti, M., and Bertazzi, P. A. (2008) *Am J Epidemiol* 167(7):847-858
3. Cavalieri d'Oro, L, Rognoni, M, Consonni, D, Pesatori, A. C., and Bertazzi, P. A. (2013) *Eur J Epidemiol* Vol. 28, Supplement 1, pag S167

Table 1 – Results of deterministic linkage between Seveso cohort and BDA.

	Zone				
	Reference	R	B	A	Total
No. present on July 10, 1976	181,559	31,643	4,821	723	218,746
% linked 2006-2014	78.3%	80.9%	80.7%	82.4%	78.7%
N. with diabetes	10,821	1,998	357	46	13,222
DM Prevalence (%)	10.1%	10.0%	11.3%	9.5%	10.1%

Table 2 - Diabetes Mellitus prevalence odds ratios (OR) and 95% confidence intervals (CI) adjusted for age and sex BDA 2006-2014

Zone	Males		Females	
	N	OR (95% CI)	N	OR (95% CI)
A	25	0.99 (0.64 – 1.53)	21	0.95 (0.60 – 1.50)
B	205	1.31 (1.12 - 1.53)	152	1,17 (0.98 – 1.39)
R	1,054	0.98 (0.91 – 1.05)	944	1.08 (1.00 – 1.16)
Non-ABR (reference)	5,801	1.00	5,020	1.00
B*	205	1.31 (1.11 -1.54)	152	1.17 (0.97 – 1.40)

* Adjusted also for arterial hypertension, cardiovascular diseases, and hypercholesterolemia (as surrogate marker for body mass index)

Figure 1

