

NERVOUS SYSTEM CANCER MORTALITY IN AN INDUSTRIALIZED AREA OF BRAZIL 1980 - 1993

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ABSTRACT - Objectives: The industrialization process and nervous system cancer (NSC) mortality in a urban region of Brazil. **Method:** From registries of the State System of Data Analysis Foundation (SEADE), 103 males deaths by NSC (ICD-9) in Baixada Santista (BS), from 1980 to 1993 were selected. Mortality ratios were calculated comparing the standardized mortality rate for ages over 10 years old (G1) and for the age group from 35 to 64 years old, in the industrialized and non-industrialized areas in three periods: 1980-1993, 1980-86, 1987-93. **Results:** A statistically significant high mortality was observed in the industrialized area, for ages over 10 in all periods and only from 1980 to 1993 for ages from 34 to 64. The highest mortality ratio occurred from 1980-86 for ages over 10 - 4.12 (CI 1.79-9.42). **Conclusion:** High mortality was probably related to the environmental and occupational exposure to many organic and inorganic chemical substances, considered carcinogenics, such as aliphatic and aromatic hydrocarbons, organochlorinated, formaldehyde, nitrogenated compounds and heavy metals, found in the port and industrial complex. We discuss the importance of case-control studies in characterizing the association of these and other risk factors in the determination of NSC.

KEY WORDS: occupational cancer, cancer mortality, cancer epidemiology, nervous system cancer; brain cancer.

Mortalidade por câncer do sistema nervoso em uma área industrializada do Brasil 1980-1993

RESUMO - Objetivo: Estudar o processo de industrialização e a mortalidade por câncer do sistema nervoso (CSN) em uma região urbana do Brasil. **Método:** Foram selecionados dos registros das Fundação Sistema Estadual de Análise de Dados Estatísticos (SEADE), 103 óbitos por CSN (ICD-9) ocorridos na Baixada Santista, no sexo masculino acima dos 10 anos, de 1980 a 1993. Calcularam-se as razões de mortalidade, padronizadas por idade, comparando as áreas industrializada e não industrializada, nos períodos de 1980-93, 1980-96 e 1987-93. **Resultados:** Observou-se excesso significante de mortalidade na área industrializada para a população acima de 10 anos, em todos os períodos - 3.11 (CI 1.84-5.32), 4.12 (CI 1.79-9.42) e 2.63 (CI 1.29-5.25). Para o grupo de 35-64 anos o excesso ocorreu apenas no período de 1980-93 - 2.46 (CI 1.20-5.11). **Conclusão:** Supõe-se que esse excesso relaciona-se à exposição ocupacional e ambiental a carcinogênicos presentes no complexo industrial-portuário como: hidrocarbonetos aromáticos, órgão-clorados, compostos nitrogenados e metais. Estudos caso-controlé são necessários para o estudo desses e de outros fatores de risco na determinação do CSN.

PALAVRAS-CHAVE: câncer ocupacional, mortalidade por câncer, epidemiologia do câncer, câncer do sistema nervoso.

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The knowledge about occupational cancer has been expanding in the last decades due to epidemiological studies and identification of genetic and environmental elements which interfere in the oncogenic process. Carcinogenic substances, produced and consumed in different ways in the industrialized societies, are risk factors that contribute to morbi-mortality of several kinds of cancer in many regions and countries in the world¹⁻³. Chemical substances occupy a surmounting position in the occupational cancer etiology, as evidenced by extensive literature^{1,3-5}.

Nervous system cancer (NSC) has been associated in epidemiological studies with lifestyle and exposure to chemical substances and occupations in the industrial work process⁶⁻⁸. However, it is difficult to approach NSC due to the low frequency and diversity of diagnosis criteria. It can be classified into malignant and benign tumors; brain cancer or cancer of other nervous structures, or in some histological categories such as astrocytomas, glioblastomas, gliomas and meningiomas^{6,8-12}. In fact, the world morbidity and mortality of NSC is low. According to Parkin's² estimative to the year 1985, NSC was the less frequently observed cancer, and was not classified among the 18 major cancers worldwide. Davis et al.¹⁰, observed increase in NSC mortality from 1968 to 1987 in several industrialized countries and they believe that this trend could be explained by improvement in diagnostic technics.

In the present investigation, part of the project "Cancer and Work" (The "Cancer and Work" project analyzes the morbi-mortality of different kinds of cancer related with the production and work process, industry, occupation and chemicals.), it was analyzed the distribution and evolution of male NSC mortality, from 1980 to 1993, in industrialized and non-industrialized areas in Baixada Santista (BS). This region presented the highest cancer mortality rate in State of São Paulo, Brazil¹³.

METHOD

The BS is an urban and industrialized region on the Southeastern coast of Brazil, next to the metropolitan area of São Paulo, which has an important metallurgical petrochemical center and the first harbor of the country. Its industries use raw materials and produce well-known carcinogenic products and input^{1,14,15}.

1. Strata

In 1994 there were 1.3 million inhabitants in the BS area, distributed in eight counties: the industrial complex (harbor and industries) including Cubatão, Santos, São Vicente and Guarujá (Stratum I); and non industrialized area (apart from that complex) including Praia Grande, Monguaguá, Itanhaém and Peruíbe (Stratum II).

In 1991 both strata had subjects living mostly in the urban areas (0.24 % living in the rural area in Stratum I and 1.29% in Stratum II)¹⁶.

2. Industrial-harbor complex

The implantation of leather, rubber, paper and cardboard paper industries in Cubatão (148 Km²), a region surrounded by the coast and by the ridge, occurred in 1912, being that complex latter integrated to the Santos harbor. In the late 50's, the petroleum refineries, several petrochemical and fertilizing industries were installed and a decade later, a steel mill plant, a chloro-alkali chemical and a Portland cement industry¹⁷.

The petroleum refinery is made of three parts including distillation and cracking, petrochemical and asphalt; other nine petrochemical industries of carbon black, styrene, ethylene and polyethylene, vinyl chloride, pentachlorophenol substituted by carbon tetrachloride, methane and formaldehyde. These industries use toxicant raw materials, intermediate and final products such as: heavy metals, fluoride and organic substances (aliphatic hydrocarbons, chlorinated aliphatic hydrocarbons, aromatic hydrocarbons and polycyclic aromatic hydrocarbons)^{1,14,15,17,18}.

According to the Social Information Annual List (RAIS), edited by Labor Ministry, from 1985 to 1993, the average employed population (excluding the retired people), working exclusively

Table 1. NSC mortality in males in Baixada Santista (Brazil) in periods 1980-1993, 1980-1986 and 1987-1993.

Rates*	Periods			Ratio 1980-86 / 1987-93	CI**	
	1980-1993	1980-1986	1987-1993			
ASMR***	2.15	2.30	1.99	1.15	0.78	1.72
TASMR****	2.95	3.46	2.48	1.39	0.83	2.35

*standardised for 1960 world population; **95% confidence interval; ***population over 10 year-old; ****population from 35 to 64 year-old

in the industrial area, was 18.9 % in Stratum I and 7.9 % in Stratum II, mostly concentrated in the local small companies. The industrial workforce lived mainly in Santos and São Vicente counties and were mostly concentrated in the steel mill and petroleum refinery areas¹⁷.

3. Mortality rates and ratios

From State System of Data Analysis Foundation (SEADE) in São Paulo State, all males death by NSC (ICD-9 191-192), above 10 years old and resident in BS, from 1980 to 1993 were selected. The reliability of the death certificates was considered taking into account that the medical care system in BS is one of the best in Brazil. Information concerning the population was also obtained at SEADE. However, it was not possible to analyze the occupation variable because, in the great majority of cases, the death certificates just registered the term retired.

Using standardization according to the world population in 1960, the age standardized mortality rates (ASMR) for individuals over ten years of age and the truncated age standardized mortality rates (TASMR) for the truncated population from 35 to 64 years of age, for the BS area and Strata I and II, in the periods: 1980-1993, 1980-1986 and 1987-1993 were calculated. It was also calculated the ratios among the mortality rates for the Strata I and II in all periods, adopting in statistical analysis a 95% confidence interval^{19,20}.

RESULTS

1. *Mortality in BS* - From 103 deaths investigated, 96 were residents in Stratum I and 7 in Stratum II. The mortality rates in the 1980-1993 period were 2.15/100 000 for the ASMR and 2.95/100 000 for the TASMR. This last group always had higher rates (Table 1).

2. *Tendency of mortality from 1980-86 to 1987-1993* - Rates decreased in this period except the ASMR in Stratum II. However, there was no statistical significance (Table 2).

3. *Comparison between Strata* - The ASMR has reflected an excess of mortality with statistical significance in Stratum I in all periods. The ratios in the periods 1980-1986, 1987-1993 and 1980-1993, were respectively: 4.12 (CI 1.79 – 9.42), 2.63 (CI 1.29 – 5.25) and 3.11 (CI 1.84 – 5.32). For the truncated group, the ratios have always been at least twice higher in Stratum I, but statistically significant only in the period 1980-1993 corresponding to 2.46 (CI 1.20 – 5.11) (Table 2).

DISCUSSION

In this study the NSC excess mortality was statistically significant in the counties of the industrialized complex (Stratum I) in the BS in relation to the areas out of it. The higher difference was observed in period 1980-86, for age group over 10 year-old, with ratio 4.12 (CI 1.79 – 9.42). Except bladder cancer, none of other cancers (lung, oropharyngeal, colorectal, hematopoietic system, pancreas, prostate) that show excess mortality in BS, presented the ratio equal or above 3²¹.

In 1991 Doll²² classified brain cancer among the 8 moderate-excess of mortality in the urban area and suggested that it could be caused by the exposure to a mixture of oils used in the urban

areas and by chemical and rubber industry worker. The author did not analyze mortality according to levels of industrialization.

The excess of NSC can be partially explained by the exposure to many chemical substances described as neurocarcinogenic, found in the production process of the BS industrial complex. The São Paulo's Environmental Sanitation Agency (CETESB)¹⁴ reported in 1980, annual tons of carcinogenic substances in the industrial waste: dregs of petrol (4,350 tons), dregs of tar (832 tons), carbon black (1,319 tons), styrene and sulfur (1,200 tons); perchloroethylene, carbon tetrachloride, hexachlorobutadiene and hexachlorobenzene (912 tons); cellulose fiber residue, kaolin, titanium oxide and aniline (360 tons); naphtha, coal tar and naphthalene (12 tons); plastic bags and polyethylene grains (1,581 tons); sodium pentachlorofenate (36 tons). Besides that, among the liquid waste there were 2,600 tons of polyethylene and polyethylbenzene and 2,938 tons of tar. In the industrial complex, among input and derivatives are identified substances with severe neurotoxic actions such as mercury in the chloro-alkali industry and manganese in the steel production. According to CETESB¹⁴ the solid waste presented 122 tons of mercury, 480 tons of mercury sulphate and 135 annual tons of molybdenum, vanadium, copper, manganese and nickel.

Epidemiological studies reinforce the importance of environmental and occupational exposure in BS area when they show an association between NSC and several jobs, occupations and substances also found in that area such as: activities highlighting the petrol, petrochemical, rubber, plastic, asphalt, metals and paper industries^{6,11,12,23-28}.

The solvents derived from chlorinated aliphatic hydrocarbons such as tetrachloroethylene, trichloroethylene, carbon tetrachloride, monochloromethane, trichloroethane and dichloromethane are carcinogenic agents^{8,9,27,29,30}. In the case-control study, performed by Heinemann et al.²⁹, six solvents derived from chlorinated aliphatic hydrocarbons, with mutagenic actions, had shown high significant association among astrocytomas and methyl chloride, in a matrix of occupational exposure. Vinyl chloride, polyurethane, polystyrene and polyethylene used as monomer and polymer substances in the plastic industry are also very important in the NSC etiology^{6,27}.

Several authors have shown that the carcinogenic agents such as: high molecular weight aliphatic hydrocarbons (gasoline, diesel oil), aromatic hydrocarbons, polycyclic aromatic hydrocarbons (PAH) and polychlorinated biphenyl, increase the risk of NSC in populational groups submitted to occupational exposure (drivers, heavy-vehicle operators) and environmental pollution^{6,7,31,32}.

In the production process in the BS industrial area there is also exposure to polycyclic aromatic hydrocarbons, due to the use of fuel in the industrial production (occupational and environmental risks) and the filling up of trucks and carts (occupational risk among drivers and the population in general). There is intense truck circulation from BS to the metropolitan area of São Paulo and vice-versa.

Besides the chemical substances, the ionizing radiations are also considered as occupational carcinogenic agents^{28,33}. Furthermore, the electromagnetic radiation have also been considered as occupational risk of NSC^{34,35}. Speers et al.³² have observed higher risk among utility workers:

Table 2. NSC mortality in males in Strata I and II in BS in periods 1980-1993, 1980-1986 and 1987-1993.

Rates*	Strata		Ratio I/II	CI**	
	I	II			
ASMR***					
1980-1986	2.60	0.63	4.12	1.79	9.42
1987-1993	2.24	0.85	2.63	1.29	5.25
1980-1993	2.43	0.78	3.11	1.84	5.32
TASMR****					
1980-1986	3.75	1.59	2.35	0.84	6.61
1987-1993	2.75	1.10	2.50	0.88	7.02
1980-1993	3.26	1.32	2.46	1.20	5.11

*standardised for 1960 world population; **95% confidence interval; ***population over 10 year-old; ****population from 35 to 64 year-old.

electricians, electronic and communication technicians. It is believed that in great number of industries in the BS area, there might occur occupational exposure to ionizing and electromagnetic radiations.

It was observed a non-significant tendency to decrease the mortality in Stratum I in population over 10 years old as well as in age group from 35 to 64. This reduction has also been observed for other sites of cancer such as oropharynge and bladder²¹. It might have been caused by the effective industrial control measures taken by governmental organization, in the BS area, from 1983 on³⁶, as shown in Table 2.

In opposition to our findings, it has been observed in many countries the tendency of increase in the incidence and mortality of the NSC in the last decades, mainly in older groups in industrialized areas. This fact has been attributed to the improvement in diagnostic techniques^{6,10,28} and exposure to carcinogenic factors^{6,7,29}. Among these, urbanization, industrialization, socioeconomic conditions, lifestyles and occupational exposure have been cited^{11,25,37}.

The positive association of NSC with several indicators that express high socioeconomic standards has been studied, highlighting among them: higher social class and status, higher educational level, self-employed professionals, businessmen and administrators^{6,8,11,27,28}. On the other hand, drinking and smoking, well-known risk factors for other kinds of cancer, are not strongly associated with NSC in most studies^{33,39,40}.

In principle, the high mortality observed by NSC in BS could not be justified by socioeconomic differences because the two Strata have similar socioeconomic conditions, typical of urban and balneal regions. On the other hand, that mortality excess could also not be explained by the tobacco use once this factor has not been considered as high risk. However, such factors must be taken into account in future studies.

The mortality excess observed in industrialized area appears to be related to the exposure to great variety of carcinogenic agents, probably in high concentration, due to inadequate spread of pollutants caused by bad ecological conditions and because of the adequate programs for the environmental and occupational pollution control in that area, were designed only from 1983 on.

Our results show the need for a deeper historical analysis of the substances used in the industrial complex in the last decades and, at the same time, of an epidemiological study of case-control morbidity. This might qualify better the possible cause associations resulted from occupational and environmental exposure, as well as identify factors related to socioeconomic conditions, lifestyles and personal behavior. Besides, it might allow the approach to individual genetic aspects of susceptibilities which may improve the knowledge of oncogenetics mechanism, yet unknown in the NSC natural history.

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