

An overview of academic studies on cancer and environmental exposures on Sfax population

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I. Introduction

While facing a rapidly increasing urbanization in parallel with its growing economy, the Tunisian city of Sfax knew an important change in the way of life of its population. This demographic transition was followed by an epidemiological transition characterized by the net decline of communicable diseases and the emergence of non-communicable diseases, particularly cancers [1]. However, there are no efficient data collection and evaluation systems established so far except the cancer registry of the south which has been last updated in 2006 [2]. Besides, the link between environmental exposures and the different types of cancer has not so far been thoroughly established among the population of the city of Sfax where the public concerns about the pollution is still rising. Therefore, this research comes to provide a synthetic overview and a critical analysis of available academic studies (MD thesis, masters' projects, PhD dissertations...) conducted around cancer and environmental exposures on the population of the city Sfax throughout the last four decades (1974-2019) especially that cancer data is the cornerstone of cancer control.

II. Material and methods

To carry out this work, a bibliographic search was first done on different databases including Pubmed, national virtual libraries such as CNUDST and local libraries of different institutions related to the University of Sfax, particularly the one of the faculty of Medicine of Sfax.

Academic studies that tackled the subject of cancer and/or environmental exposures on the population of the city of Sfax from the 11th of December 1974 until the 30th of April 2019 were included, eliminating all studies whose population was outside of Sfax governorate or whose subject was not about either cancer or environmental exposures.

The second step was the development of the criteria specifying the attributes (variables) that were swarmed in an Excel table:

- Related to the study: index, start and end dates, duration, total number of cases
- Epidemiological features: age, gender, geographical origin (% from Sfax)
- Exposition to tobacco, alcohol and environmental carcinogenic agents

The selected studies were then coded and classified according to carcinogenic agents, cancer localizations, period of the study as well as its duration and method.

Finally, statistical analysis of the data was conducted followed by a critical analysis.

III. Results

Among 4542 MD theses and 1347 masters' projects publically available in the faculty of Medicine of Sfax, only 72 MD theses (1.6%) and 9 masters' projects (0.7%) were relevant to the selection criteria.

A. Classification of the studies by carcinogenic agents:

Only 17 studies among those 81 selected ones explored the exposure to 35 environmental carcinogenic agents. They included 16 MD theses (22.2% of the selected ones and 0.4% of the total number of conducted MD thesis in the faculty of Medicine of Sfax) and 1 masters' project (11.1% of the selected ones and 0.07% of the total number of masters' projects conducted in the faculty of Medicine of Sfax).

Other than one MD thesis entitled which explored different cancer localizations at the same time, each of the other 16 studies explored one cancer localization at a time including: breast, uterus, lung, thyroid, larynx, kidneys, blood (chronic myeloid leukemia) and skin (melanomas).

B. Classification of the studies by cancer localizations:

66 studies had each explored a specific different localization of cancer in the human body. They included 65 MD theses (90.3% of the selected ones and 1.4% of the total number of conducted MD thesis in the faculty of Medicine of Sfax) and 1 masters' project (11.1% of the selected ones and 0.07% of the total number of masters' projects conducted in the faculty of Medicine of Sfax).

In those 66 studies, 26 localizations of cancer were mentioned in 10 different systems: bone, skin, blood, respiratory, breast, genital, urinary, digestive, oral cavity and thyroid. Both the respiratory and the digestive systems were the most studied (19.7% of the total 66 studies each) while the least studied systems were the

bone (1.5%) as well as the skin and the thyroid (3% each) (Figures 1).

C. Classification of the studies by the study period

While taking into account the starting date (in year) of each selected study, we found out that most studies were carried out in the nineties (Figure 2).

Nine studies did not mention the starting date; this includes 7 MD thesis (9.7% of the selected ones) and 2 masters' projects (22.2% of considered master studies).

Concerning the duration in years of the selected studies, we found that more than the half has a duration between 5 and 15 years (Figure 3).

No information was given on the duration for 11 studies including 9 MD thesis (12.5% of them) and 2 masters' projects.

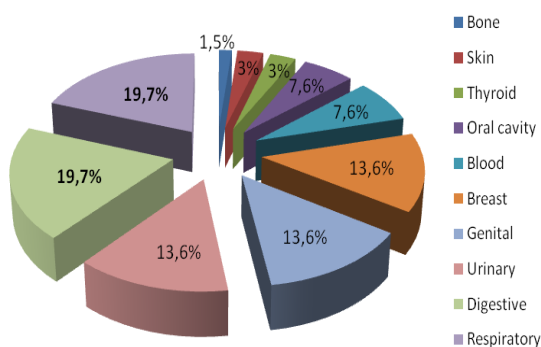


Figure 1: Studies' distribution by cancer localizations

Number of the studies

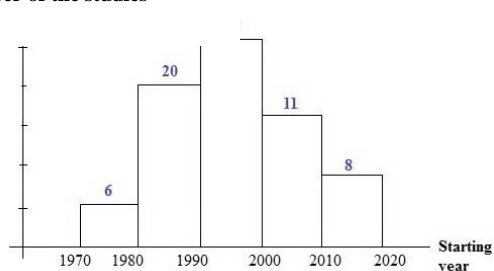


Figure 2: Studies' distribution by the period of their start

Number of the studies

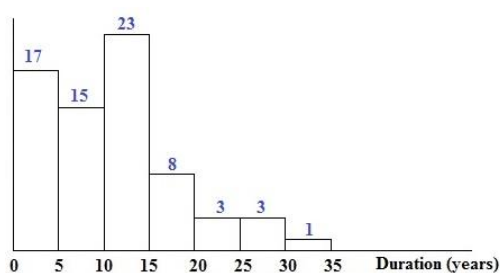


Figure 3: Studies' distribution by their durations

E. Classification of the studies by their methodology:

All of the 81 selected studies were observational and retrospective. Their majority is descriptive (93.8%) including 68 MD thesis (94.4% of the 72 selected ones) and 8 masters' projects (88.9% of the 9 selected ones) (Table I). The majority of the 76 descriptive studies were case series (88.2% of the 72 selected ones) including 65 MD theses (90.3%) and 2 masters' projects (Table II).

Table I: Types of the selected 81 observational studies

Type of the study	Number of MD thesis	Number of masters' projects
Descriptive	68	8
Analytical :		
- Case/control	2	0
- Exposed/non-exposed	1	0
Literature review	1	1

Table II: Sub-types of the descriptive studies

Type of the study	Number of MD thesis	Number of masters' projects
Case series	65	2
Cross-sectional surveys	2	3
Ecological studies	1	3

F. Epidemiological study:

While taking into account the classification of the selected studies by the different cancer localizations, we found out the following epidemiological results (Table III):

- A masculine predominance is observed in the majority of the studied cancers, except for three localizations, where a feminine predominance is observed (breast, skin and gall bladder).
- As for the mean age, the majority of the studied cancers occurred after 50 years, except for 3 localizations in which cancer occurred after 40 years (nasopharynx, blood and thyroid) and the testicles cancer which occurred at younger ages, around 30 years.
- Concerning the geographical origin, only 21 studies (25.9%) distinguished rural from urban one and only 39 studies (47.5%) mentioned the number of cases originating from Sfax region, including 36 MD thesis and 3 masters' projects; it is noteworthy that almost all studies about cancer that have been made in the faculty of Medicine of Sfax did not mention the origin, but it can be deduced that they concern the Sfax region.

- Only 14 studies (17.3%) explored the occupation of the studied cancer cases. They include 11 MD thesis (15.3%) and 3 masters' projects (33.3%). Among those 14 studies, only 9 ones (11.1%) explored specific types of cancer in 2 systems: the respiratory system and blood. They included four localizations of cancer: lung, glottis, larynx and blood. The most prevalent occupational class in chronic myeloid leukemia and larynx are farmers.

Among the separately studied 26 cancer localizations, the geographical origin was not specified in 10: thyroid, bone, liver, gall bladder, urethra, bladder, pancreas, oral cavity, cervix and penis. As for the other 16 cancer localizations, not all related studies explored this aspect.

While considering the organ-specific studies (explored only one organ), the total number of cases of cancer from Sfax was 1481. Their distribution among the different 16 cancer localizations (Table III) could be better represented when merging the organs in 8 systems (Figure 4).

Most of the cancer cases from Sfax are explored in the studies that investigated the respiratory system (38%) as well as the breast (36%), making the rest of the cancer localizations a minority of 26% in total (Figure 4).

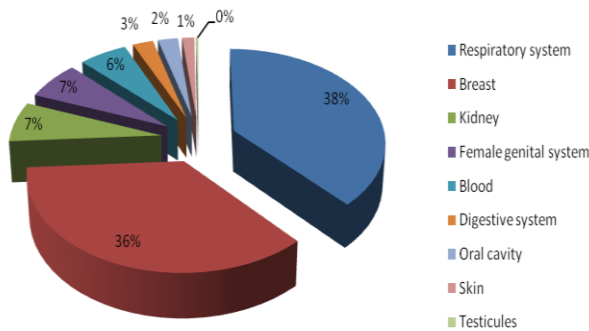


Figure 4: Distribution of the cases originated from Sfax by cancer localizations

G. Cancer-environment potential relation in Sfax city:

Among the 14 studies that explored the occupation of the studied cancer cases, only 11 mentioned the percentage of cancer cases originated from Sfax (13.6%). They included 9 MD thesis (12.5%) and 2 masters' projects. 7 studies among them explored one cancer localization at a time covering only 2 systems (the respiratory system and blood) while exploring 4 cancer localizations (Table IV): larynx, lung, glottis and blood (chronic myeloid leukemia). Among the 17 studies that explored the exposure to the different environmental carcinogenic agents, only 13 explored the cancer cases originated from Sfax (13.6%). These studies were all MD thesis. 11 among those studies

explored one cancer localization at a time (Table V): larynx, kidney, skin (melanoma), blood (chronic myeloid leukemia), breast and endometeter.

Table IV: Studies exploring occupations and cancer cases from Sfax

Cancer localization	Number of the concerned studies/number of all studies in that localization	Total number of cases in the concerned studies	Cases from Sfax
Glottis	1/1	13	8
Larynx	2/3	Study 1: 180	104
		Study 2: 215	137
Blood	2/5	Study 1: 50	24
		Study 2: 93	37
Lung	2/5	Study 1: 60	31
		Study 2: 24	15

Discussion

While commenting the results of this overview, we should keep in mind the lack of information in the selected studies (particularly the absence of the individual data for each subject) as well as the lack of homogeneity in the data collection process between those studies which made it impossible to conduct any analytical tests proving the cause to effect relation between environmental exposures and cancer.

Nevertheless, the outcome of our study showed that the design of the majority of the 81 selected studies (93.8%) was retrospective, observational and descriptive. When it comes to the exposure to carcinogenic agents, which are over 400 according to the International Agency for Research on Cancer (IARC) in 2007 [3], only 35 carcinogens were qualitatively explored by 17 studies (21% of the 81 selected studies) without quantitatively measuring the amount of exposure per person. Moreover, the design of most of the descriptive studies was case series which is a report on the characteristics of a group of subjects who have the same condition. Consequently, common features may suggest hypothesis, but these need to be tested with an analytical study before an association or a causal relation can be accepted as valid. As for the 5 cross-sectional surveys, they only provided a "snapshot" of the risk factors and the detected cases of cancers simultaneously in a defined population with respect to both the exposures and the diseases. Thus, this study design leaves us with two main disadvantages:

- The absence of clarity in the temporal relationship between the exposure and the disease: which came first?

Table III: Gender, age and geographical origin by cancer localization

Cancer localization	Number of the concerned studies	Total number of cases in all studies*	Women/Men (%)	Mean age (years) [Min-Max]	Origin: cases from Sfax/ total studied cases
Lung	5	534	8.8/91.2	60.7 [57.8 – 62.8]	46/84
Colorectal	3	120	44.2/55.8	60.0 [56.8 – 62.9]	19/33
Breast	9	1539	99.7/0.3	54.1 [49.0 – 70.0]	529/667
Thyroid	2	187	48.7/51.3	44.0	-
Stomach	2	54	35.2/64.8	59.0	18/41
Skin	2	60	61.7/38.3	59.5 [57.0 – 62.0]	22/40
Bone**	1	47	40.4/59.6	-	-
Blood	5	257	45.2/54.8	44.6*** [33.0 – 53.0]	86/222
Liver	1	25	20.0/80.0	60.0	-
Gall bladder	4	215	70.2/29.7	63.2 [61.7 – 64.8]	-
Kidney	5	139	48.9/51.1	59.1 [31.6 – 64.7]	102
Urethra	2	23	13.0/86.9	67.3 [63.5 – 71.0]	-
Bladder	1	24	16.7/83.3	64.0	-
Pancreas	2	112	32.4/67.6	63.3 [58.5 – 68.0]	-
Salivary glands	2	68	52.9/47.1	55.4 [54.7- 56.0]	20/30
Oral cavity	1	100	32.0/68.0	65.5	-
Glottis	1	13	00.0 /100	57.7	8/13
Nasopharynx	2	205	24.6/75.4	41.3 [41.0 – 43.0]	42/42
Larynx	3	591	4.4/95.6	63.2 [66.7 – 60.0]	241/395
Tongue	1	25	52.0/48.0	56.0	16/25
Superior Aero Digestive Ways	1	379	12.7/87.3	61.0	230/379
Testicles	3	145	0.00/100	34.4 [27.6 – 39.0]	4/6
Endometer	3	248	100/00.0	58.0 [57.5 – 59.0]	80/97
Cervix	1	15	100/00.0	55.9	-
Vulva	1	27	100/00.0	67.0	18/27
Penis	1	4	100/00.0	54.0	-

* The total number of studied cases in each line could not reflect the real number of the cases as the studies around the same localization could use the same serials in the same hospital.

** The majority of the 47 cases of osteosarcomas (68%) were children and teenagers aged between 10 and 20 years old.

*** The mean age for blood cancers was calculated from only 4 studies which explored only adult cancer cases. The fifth study that explored acute lymphoblastic leukemia in children did not specify the mean age for the 35 studied cases. However, it precised that the majority of cases (60%) were aged between 2 and 8 years old.

- The tendency to identify prevalent cases of long duration since people who die quickly or recover

quickly or who are no longer employed in a particular occupation are less likely to be identified.

This means that over the four last decades, no prospective cohorts were done to follow up exposed subjects to known environmental carcinogenic agents in

the Tunisian city of Sfax in order to prove the causality link between these exposures and the development of the different types of cancer in the population. This may be explained by the long period of time a cancer takes to develop after an environmental exposure to a carcinogenic agent [4] and also by the prohibitive cost of funding studies that collect exposure data decades before the onset of disease [3].

However, this overview highlights that the period of most of the 81 selected academic studies which were all retrospective ones was between 10 and 15 years and that only 39.5% of the total number of the selected studies covered a period of less than 10 years. These facts sustain the explanation suggested previously but also imply the possibility of conducting prospective cohorts following exposed subjects for over a decade.

In addition, the fact that most of these studies (88.2%) were observational descriptive case series and that the year of the starting date of most of them (56.7%) was between 1980 and 2000 with a slight increase from the 80ies to the 90ies, imply that research efforts at the faculty of Medicine of Sfax became more focused on the subject of cancer only when incidence rates of cancer have increased in most countries since 1990 [5] as well as when the ministry of health of Tunisia implemented cancer registries in 1997/1998 [2,6].

The decrease of the number of studies around cancer as well as environment in the faculty of Medicine of Sfax from 2000 to 2010 as well as from 2010 to the present is in fact in parallel with the absence of any updates of the Tunisian cancer registry of the south since 2002 [2].

Although thyroid is, according to the IARC, one of the most common localizations of cancer among females [7], it was among the least studied cancer localizations in our overview as only 3% of the selected studies explored it (Figure 1). Not to mention that in the urinary system, the prostate which is one the most frequent localizations of cancer among males (globally the second after the lung according to the IARC [7] and locally the third according to the cancer register of the south [2]) was not studied separately in any academic study in this overview.

Conclusion

This work comes to provide a synthetic overview of 81 academic studies conducted around cancer and environmental exposure to 35 different carcinogenic agents in the Tunisian city of Sfax throughout the last four decades, mostly from the faculty of Medicine of Sfax.

The absence of any prospective studies along with the low percentage of analytical studies (only 3 among the 81 selected ones) along with the lack of homogeneity in the collected data from medical files even among the same localization of cancer were all alarming facts requiring a better quality research and data collecting system that would have real impact on policy making. Different recommendations were thus suggested:

Further studies should be conducted around the subject of cancer in a preventive approach in addition to the curative one. This means that efforts of health professionals should be joint with researchers from other fields such as ecologists and biologists in advance of the occurrence of the disease while quantitatively and not only qualitatively measuring the exposure to known carcinogens in the different settings where physical, chemical or biological carcinogenic agents could be found in the environment and not only in the work place.

Moreover, in order to provide stakeholders with timely estimates to guide policy efforts in cancer prevention, screening, treatment, and palliation, there should be a certain centralization of information such as through the establishment of the digital medical folder that should be accessible at any healthcare facility nationally or regionally and through the establishment of a common questionnaire used by doctors when taking the history of patients suffering or not from cancer. This would make research efforts more harmonized and the creation of big databases possible thus improving the existing data collection system.

Table V: Studies exploring cancer cases from Sfax and exposure to environmental carcinogenic agents

Cancer localization	Number of the target studies/number of all studies	Total number of cases in the target studies	Cases from Sfax	Exposure to carcinogens (%)
Larynx	2/3	215	137	Phosphate (4, 9%)
		180	104	Phosphate (4, 7%)
Kidney	1/5	20	10	Solvents (10%)
Skin	1/2	40	22	Magnetic fields (20%)
		264	205	Contraception (7, 3%)
Breast	3/9	100	74	(18%)
		108	99	(56%)
Endometrial	2/3	52	42	(7, 7%)
		45	38	(2, 2%)

			Solvents (3, 5%)
		37	Colorants (3, 5%)
			Insecticides (15 %)
		93	Phosphate (38 %)
			Insecticides (34 %)
			Solvents (30 %)
			Ionizing radiations (26 %)
Blood	2/5	24	UV Radiations (22, 5 %)
			Herbicides (20 %)
		50	Household wastes (20 %)
			Colorants (18 %)
			Acid-Base (4 %)
			Explosives (2 %)
			PVC (2 %)

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