STUDYING THE EVIDENCE OF COMPLEXITY OF INTERACTION BETWEEN ENVIRONMENTAL, OCCUPATIONAL AND HOST CANCER RISK FACTORS IN AN AREA WITH SUSPECTED CANCER CLUSTER IN EGYPT

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ABSTRACT

Background: Cancer is a generic term for a large group of diseases that can affect any part of the body with rapid creation of abnormal cells that grow beyond their usual boundaries, and can metastasize. The aim of this study was to explore the feature of the problem of cancer among Wady El Mollak citizens to add to research a new study in the field; to determine possible risk factors which may be responsible for horrible problem and the objectives were to assess the magnitude of the problem; to identifying the possible risk factors through comparing with comparable area. **Subjects and Methods**: Multi method research including case control study and ecological study were conducted at El-Mollak village in Sharkia Governorate, in November 2012. Cases of cancer were sixteen (N=16) at El Mollak village, their features were studied and matched, control group (N=16) selected randomly from a nearby village where no symptoms of cancer. A pre-coded pre-constructed questionnaire was used to collect the relevant data from cases and their controls. The ecological part of this study was done through searching the environmental risk factors and linking them to the cases and through reviewing the results of samples taken from water canal, tap water and soil of El Mollak village. **Results:** It was found that farming occupational exposure and pesticides exposure are statistically significant in the case group. Eating fish is statistically higher among cases than among controls. Environmental factors including; trench waste disposal, living near electrical fields and military croups are highly statistically significant among cases than among controls ($P< 0.01$). Presence of relatives with similar cancer or other cancers are statistically significant in the cases group. **Conclusions and Recommendations:** Cancer risk results from different complex interaction of host factors with environmental and occupational exposure. So need exists to revitalize comprehensive global cancer control policies by incorporating primary interventions against the modifiable cancer risk factors.

Key words: cancer, cluster, risk factor, occupational and environmental factor.

INTRODUCTION

Cancer is a generic term for a large group of diseases that can affect any part of the body with rapid creation of abnormal cells that grow beyond their usual boundaries, and can metastasize. The estimated global burden of cancer amounts to some 12,667,400 new cancer cases worldwide in 2008 [(1)], and continue in rising, with an estimated 13.1 million deaths in 2030 [(2)].

Many risk factors can increase a person's chance of developing cancer; however cancers are primarily an environmental disease with 90–95% of cases attributed to environmental factors and 5–10% due to genetics [(3)]. Environmental factors, as used by cancer researchers don't merely mean pollution but any cause that is not inherited genetically. Common environmental factors that contribute to cancer death include tobacco (25–30%), diet and obesity (30–35%), infections (15–20%), radiation (both ionizing and non-ionizing, up to 10%), stress, lack of physical activity, and environmental pollutants [(4)].

These factors can directly damage genes or combine with existing genetic faults within cells; they can interfere with gene repair mechanisms, hormone production/function, or produce chronic inflammation to cause cancer. It is nearly impossible to prove what caused a cancer in any individual, because most cancers have multiple possible causes [(5)].

Unfortunately, there is evidence that cancer susceptibility resulting from environmental exposures may be inherited by a child when a carcinogen causes germ cell genetic damage in exposed parents [(6)].

In order to adopt effective preventive measures and regulatory actions, a comprehensive investigation of cancer etiology is crucial. Variations and fluctuations of cancer incidence in human populations do not necessarily reflect environmental pollution policies or population distribution of polymorphisms of genes known to be associated with increased cancer risk [(7)].

It's challenging to provide evidence that environmental exposure to complex mixtures of pollutants results in increased cancer risk whether by human epidemiologic studies or by experimental studies conducted in vitro or in laboratory animals. The mechanisms by which environmental contaminants contribute to cancer risk, and particularly how they interact, remain largely under investigated in human [(8)]. As there is still a lack of epidemiological researches in this area to have sufficient evidence, **So, the aim of this study was:** To explore the problem of cancer among Wady El Mollak citizens to add to research a new study in the field; to determine

possible risk factors which may be responsible for this problem and the objectives were to assess the magnitude of the problem and to identifying the possible risk factors through comparing with comparable area.

SUBJECTS AND METHODS

I. Study setting and design:
A case control study and an ecological study were conducted at El-Mollak Village in Sharkia Governorate in November 2012.

11. Study population:
It includes two groups:
a- Case group: included all cases of cancer at El Mollak village Sharkia governorate sixteen (N=16).
The inclusion criteria (Case definition): All patients who proved to have cancer by medical records and investigations and had or on current cancer treatment. Different types of cancer were cancer bladder, cancer breast, leukemia and cancer thyroid.
b- Control group: included (N=16) healthy individuals selected randomly from nearby village and have no symptoms of cancer. They were matched to the cases regarding age and sex.
Exclusion criterion of control group: Any person who has been suspected of cancer at the time of the study.

B- Ecological study:
An ecological study was done through searching the environmental risk factors and linking them to the cases and through reviewing the results of samples taken from water canal, tap water, soil and fertilizers of El Mollak village.

III- Methods of data collection:
Case control:
1. Data were collected about case study information through:
* Reviewing the medical records at El Mollak village, Sharkia governorate cases for detection of:

- The number and diagnosis of cancer cases came from El-Mollak village.
- The results of the initial laboratory investigations that done for cases.
- The management protocols that were carried out to the cases.

The results were recorded for each case.
***** Environmental assessment: which done through reviewing the results of samples taken from water canal, tap water, soil and used fertilizers of El Mollak village.
2- Assessment of the risk factors for the suspected cases: this was carried out through:
(a) A pre-coded pre-constructed questionnaire to collect the relevant data from cases and their controls about:
- Personal and socioeconomic data (socioeconomic standard is measured according to [9].
(
- Hygienic and cultural habits as washing hands before and after meals, children playing with mud, house hygienic conditions and insecticides usage.
- **Nutritional status**; eating food rich in vitamins, minerals and daily food intake.
-**Occupational exposure** as working or dealing with insecticides, hormonal fertilizers or electrical power fields.
- **Environmental risk factors** as living or working near factories or high power electrical fields
- **Present and past histories** of any symptoms related to cancer type.
- **Family history** of cancer.

Ethical issues:-
Official permission was obtained from faculty of Medicine and Community Medicine Department' Ethical Committee. An informed consent had been obtained from every participant in the study. Also an informed written consent had been obtained from children parents.

IV- Data management:
The collected data were completely reviewed.

- Then the data were computerized and statistically analyzed using SPSS (Statistical package for social sciences) version 11.0.
- Quantitative data were represented as range, arithmetic means and standard deviations **(X SD)** [10].
- Qualitative data were represented as frequencies and percents, Chi-square test ($\chi 2$) was carried out for calculating significant differences between the qualitative data; when appropriate otherwise "Fisher's exact test" was done when expected cell is less than five [11].
- A result was considered statistically significant when the significant probability was less than 0.05 ($P < 0.05$).

RESULTS

There are no statistical significant differences as regard general characteristics of the studied groups except for occupation, occupational exposure in farming and pesticides Exposure as shown in **table (1)**. There are no statistical significant differences between cases and their controls in breakfast and dinner, while those who eat fish are statically higher among cases than among controls ($P<0.001$) **(table 2)**.

Both cases and their controls use tap water for drinking. Neither cases nor their controls live or work near factories or quarries. Trench waste disposal, live near electrical fields and near

military croups are highly statistically significant among cases than among controls (P< 0.01) **(table 3). In table (4)** 43.8 % of cancer cases have similar cases of cancer in family about 28.6 % of cases have relatives either brothers, son or another wife suffered from cancers with diseases are statistical significant compared to their controls while 75.0 % have no chronic diseases, 14.3 % of cases have past history of biliharziasis, DM, arthritis and hepatitis (HCV) which did not statistically differ from controls. 56.2 % had no treatment while 6.2 % had chemotherapy, irradiation, liver drugs, DM drugs, cardiac drugs, interferon on the other hand 50.0 % had surgical treatment with mean values of years (1.3 ± 1.8).

Results of samples taken from canal water, tap water and soil showed no proved chemical carcinogen or radiation, however samples from fertilizers (Pesticides) were suspicious

Table (1): Socio demographics of the studied cases compared to controls.

Characteristics'	**Cases (N=16)**		**Controls (N=16)**		**χ2**	**P-value**
Sex	**No**	**%**	**No**	**%**		
Male	6	37.5	8	50.0		
Female	10	62.5	8	50.0	0.50	0.47
Age						
X (SD)	49.1±17.9		38.7±16.5		1.7	0.1
Range	9.0-85.0		12.0-77.0			
Age groups	**No**	**%**	**No**	**%**	**χ2**	**P-value**
<20 years old	1	6.2	1	6.2		
20-40 years old	4	25.0	8	50.0	2.2	0.3
>40 years old	11	68.8	7	43.8		
Education						
Illiterate	13	81.2	9	56.2		
Read& write	2	12.5	2	2.5		
Moderate edu.	1	6.2	2	2.5	4.1	0.25
high edu.	0	0.0	3	18.8		
Occupation						
Farmers	15	93.8	0	0.0		
Other than farmers	1	6.2	16	100.0	28.3	0.000**
Occupational exposure in farming						
Yes	10	62.5	0	0.0	14.5	0.000***
Pesticides Exposure						
Yes	8	50.0	0	0.0	Fisher Exact test	0.002**
How many years	21.8 ±9.1		--	---		
Hours of daily exposure	11.7±2.2					
Smoking Habit:					t-test	P-value
Cigrates/day	26.6±11.5		22.3±16.6		0.37	0.73
How many (years since starting smoking)	30.0±24.1		8.0±1.7		1.5	0.2
	No	**%**	**No**	**%**	**χ2 (Odds ratio, CI, 95 %)**	
Both cigratte and Goza	7	43.7	3	18.8	2.3 (3.37) (0.55-22.8)	0.12

Table (2): Nutritional habits among studied groups.

Characteristics'	Cases (N=16)		Controls (N=16)		$\chi 2$	P-value
Breakfast	**No**	**%**	**No**	**%**		
Milk and Eggs+vegetables	16	100.0	16	100.0	----	-----
Lunch						
Fish	13	81.2	3	18.8		
Canned food	1	6.2	3	18.8	12.5	0.002**
Meat and bread	2	12.5	10	62.5		
Dinner						
Cheese and milk	15	93.8	16	100.0	Fisher Exact	1.0
Canned food	1	6.2	0	0.0		

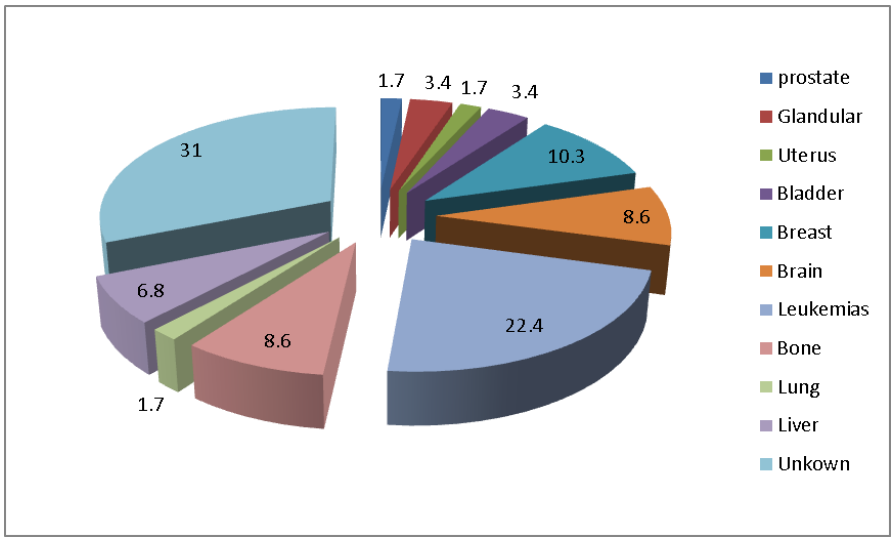
Table (3): Environmental profile of studied cases.

Characteristics'	Cases (N=16)		Controls (N=16)		$\chi 2$	P-value
Water source	**No**	**%**	**No**	**%**		
Tab water	16	100.0	16	100.0		
Underground	0	0.0	0	0.0	---	----
Sewage disposal						
Trench	16	100.0	0	0.0		
System	0	0.0	16	100.0	Fisher Exact	0.000***
Factories						
No	16	100.0	16	100.0		
Quarries						
No	16	100.0	16	100.0		
Electric fields						
Yes	7	43.7	0	0.0	Fisher Exact	0.01**
No	9	56.3	16	10.0		
Emission Sources:						
Nuclear reactor	0	0.0	0	0.0		
Hospital	0	0.0	0	0.0		
Bakery	16	100.0	0	0.0	Fisher Exact	0.000***
Military croup						
1-2 kilometer far	16	100.0	0	0.0	Fisher Exact	0.000***

Table (4): Medical profile of the cases.

Characteristics'	Cases (N=16)		Controls (N=16)		χ2	P-value
Similar cases in the family	**No**	**%**	**No**	**%**		
Yes	7	43.8	0	0.0	Fisher Exact	0.01**
Relatives had cancer						
Another wife	2	28.6	0	0.0		
Brother	2	28.6	0	0.0	Fisher Exact	0.01**
Son	1	14.3	0	0.0		
Cousin	2	28.6	0	0.0		
Chronic diseases						
None	12	75.0	13	81.2	Fisher Exact	1.0
Bilharzias	1	14.3	0	0.0	Fisher Exact	1.0
DM	1	14.3	1	14.3	Fisher Exact	1.0
Arthritis	1	14.3	1	14.3	Fisher Exact	1.0
Hepatitis (HCV)	1	14.3	1	14.3	Fisher Exact	1.0
TTT						
None	9	56.2	---			
Chemotherapy	1	6.2			---	---
Irradiation	1	6.2	---			
Liver drugs	1	6.2			---	---
Drugs for DM	1	6.2	---			
Cardic drugs	1	6.2			---	---
Interferon	1	6.2	---			
Analgesics	1	6.2			---	---
Surgical	8	50.0	---			
When (Years)	1.3±1.8				---	---

Figure (1): Types of registered cancer cases.



DISCUSSION

In order to adopt effective preventive measures and the associated environmental regulatory policies and actions, a comprehensive investigation of cancer etiology is crucial [12].

The cases profiles showed mean age of (49.1±17.9) and about two times of them were female and more than 80% were illiterate. Cancer used to be regarded as an aging-related disease, as with longevity there is both increased opportunity for DNA damage and longer exposures to potential carcinogens [13].

Previous study done by [12], observed increased cancer rates among females nearly everywhere in Europe. These finding might be due to increased rate of cancer breast which is the most frequently occurring cancer in females. Also, it was known previously that (just being a woman is the biggest risk factor for developing breast cancer).

As regard to the educational level, previous study shown inverse association between educational as an indicator of socioeconomic status (SES), and occurrence of cancer at several (but not all) anatomic sites [14]. However, other studies reported higher incidence of cancer among higher educated individual. The differences in cancer risk associated with education (or SES) likely reflect differences in financial resources, lifestyles (including carcinogenic exposures), and access to healthcare services that influence cancer mortality risk [15].

Considering personal characteristics, this study showed that occupation and smoking habit were significantly different between cases and control.

As regard the occupation, although farmers usually considered at lower risk of cancer than the general population, possibly because of healthier lifestyles (i.e., lower smoking prevalence, more physical activity), the present study showed that the majority of cases (93.8%) were farmers which is consistent with previous studies [16] which concluded increased risk of cancer in farmers, This increased risk could be attributed to farm exposures to some carcinogens during their work practices such as pesticides, nitrate, solvents and viruses [16].

Moreover, the information on the participants' involvement in raising some crops and livestock (which we don't have) might clarify these findings. Also, farmers are frequently exposed to solar radiation at the midday hours when the sun is strongest and numerous epidemiological studies, suggested that lifetime accumulation of exposure to sunlight, produce change in the gene or chromosome of one or more cells and increased the risk of squamous skin cancer, non-Hodgkin lymphoma [17]. Similarly, our study reported 22.4% of cases with non –Hodgkin lymphoma and leukemia.

Furthermore, [18] mentioned in their study in the Nordic Countries, that knowledge of cancer risk according to occupational affiliation is an essential part of formatting preventive actions aimed at the adult population. The types of cancer that have most commonly been linked with occupational exposures and for which evidence is strong, are those of the lung, urinary bladder, mesothelioma, larynx, leukaemia, angiosarcoma of the liver, nose and nasal cavity and skin [19] which is relatively similar to our cancer types in this study.

Different epidemiological studies reported that pesticides are carcinogenic, (e.g., organchlorines, creosote, and sulfallate) while others (organchlorines DDT, chlordane, and lindane) are tumor promoters. Moreover, some contaminants in commercial pesticide formulations also may pose a carcinogenic risk [20].

Considering the occupational exposure to pesticides among cases, it was found that half of cases occupationally exposed to pesticides with mean values of 21.8 years of usage, and 11.7 hours daily. Similarly, WHO, 2011 reported that agricultural exposures to pesticides, indoor, outdoor air pollution and chemical contamination of water can constitute cancer-causing factors present in our living and working environment and the expected impact of occupationally-related cancers in low- and middle-income countries is higher due to lack of or less stringent monitoring of worker protection, less occupational hygiene and safety, and child labor.

Regarding cigarette smoking, it has been clearly and unambiguously identified as a direct cause of cancers of the oral cavity, oesophagus, stomach, pancreas, larynx, lung, bladder, kidney and leukaemia, especially acute myeloid leukaemia [21]. Also, available evidence suggests that water pipe smoking (e.g. hookah, shisha, narghile) is associated with many of the known risks of tobacco smoking, particularly cancer [22].

Despite a small sample size, the current study showed that one eights of the cases are smokers, one quarter of them were shisha consumers, and 43.7% are both cigarette and shisha smokers but with no significant difference compared to control group.

Similarly, a study published in December 2011 estimated that smoking causes nearly a fifth of all cancer cases in the UK [23], in addition, the interaction between smoking and other harmful exposures can result in a much greater risk in people exposed to both. Also, a fairly recent meta-analyses show that exposure to environmental

tobacco smoke at work or in the home increases the risk of lung cancer among non-smokers by about a quarter, while heavy exposure at work doubles the risk [24, 25].

Regarding the nutritional profile**,** world health organization documented that as much as 30% of all cancer cases are linked to poor dietary habits and the proportion reaches 70% for cancers of the gastrointestinal tract [26]. Similarly, [27] reported that Smoking, alcohol use, and low fruit and vegetable intake were the leading risk factors for death from cancer worldwide and in low-and-middle-income countries.

Fish is high in protein and omega-3 fatty acids. But concerns have been raised in recent years about chemicals found in fish from environmental pollution, including mercury, PCBs and dioxins.

In the current study, it was found that those who eat fishes were statistically higher among cases than control groups (p<0,002). This could be explained by fact that some fishes can be poisoned with PCBs and dioxins, which are carcinogenic as shown with previous studies [28]. On the other hand, some authors found that the benefits of eating fish far outweighed the potential cancer risks from these chemicals, as the levels of PCBs and dioxins in fish species are low, similar to other commonly consumed foods such as beef, chicken, eggs, and butter and the possible health risks of these low levels of PCBs and dioxins in fish are only a small fraction of the much better established health benefits of the omega-3 fatty acids.

Moreover, the study also points out that only 9% of the PCBs and dioxins in the U.S. food supply come from fish and other seafood; more than 90% comes from other foods such as meats, vegetables, and dairy products [29].

Environment is a known contributor in cancer. Annually, roughly 19% of all cancers are estimated to be attributable to the environment, including in work settings, resulting in 1.3 million deaths [30]. Several geographical comparison studies have investigated cancer mortality and incidence around waste sites. Our results showed highly significant difference (p=0.000) between the studied groups regarding trench sewage disposal. This is in accordance with previous study that demonstrated that critical deficits in basic water supply and sewage treatment infrastructure have increased the risk of exposure to infectious and parasitic disease and to a growing volume of industrial chemicals, heavy metals, and algal toxins which most of them are carcinogenic [31].

In contrast to previous study by [32] which demonstrated lower risk of developing cancer and mortality among personnel exposed to military areas compared to the general population, this study showed highly significant difference between cases and control group regarding living near military area. This difference could be attributed to complete absence of military exposure among control group.

Also, this study showed highly significant difference between cases and control group regarding bakery exposure which is consistent with previous study which reported high risk of developing nasal and other respiratory tract cancers and attributed it to flour dust exposure [33].

In addition, the present study showed that there are electric fields about 3kms away from participants' residence which may be one of the contributing factors for cancer. Similarly, In June 2001, an expert scientific working group of IARC published studies related to the carcinogenicity of static and ELF electric and magnetic fields. The interaction with tissues by inducing electric fields and currents in them is the only established mechanism of action of the electric field. However, the electric currents induced by ELF fields commonly found in our environment are normally much lower than the strongest electric currents naturally occurring in the body such as those that control the beating of the heart [34].

Family history of cancer is reported by about 43.8% of cancer cases in the current study and 28.6% of cancer cases confirmed occurrence of cancer in their relatives of first and second degree which are highly statistically significant compared to control group.

These findings are in agreement with previous study by [35] which demonstrated that first degree family members are capable of accuracy in reporting chronic illnesses such as cancer among their immediate family members while accuracy declines when the definition of family is expanded. In addition, the current study reporting of cancer in another wife previously lived in the same house may be referred to environmental factors.

Limitations of the study:

Small sample size, occupational exposures in this study were self-reported and this might bias results. Budget constrains which limit further detection of various cancer risk factors.

Conclusion and recommendations:

Cancer risk results from different complex interaction of host factors with environmental, occupational exposure collected during their life. So Opportunities exist to revitalize comprehensive global cancer control policies by incorporating

primary interventions against the modifiable cancer risk factors.

Competing interests:

The authors declare that there are no competing interests. This research paper was financed totally by the authors of the study.

Contributors:

All the research team designed the study and the questionnaire, determined the objectives and conducted the practical phase, Marwa Bayomi wrote the introduction, Mona Mohamed Abou El khair wrote the methodology and analyzed the data statistically, Marwa zalat discussed the results and wrote the conclusions and recommendations and Ghada Salem wrote the abstract and references. All authors revised the manuscript and have seen and approved the final version.

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