



Received on 03 April 2020; received in revised form, 09 April 2021; accepted, 13 April 2021; published 01 May 2021

THE IMPACT OF CARCINOGENIC CHEMICAL USE AMONG CARDAMOM FARMERS AND THE PREVALENCE OF CANCER IN IDUKKI DISTRICT, KERALA

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Keywords:

Carcinogen, Cardamom, Cancer, Chemical pesticides, Idukki, Prevalence

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ABSTRACT: The prevalence of cancer is drastically increasing among cardamom farmers using chemical pesticides in Idukki district. The chemicals, mainly Organochlorine and organophosphates, result in various disease conditions. The main aim of the study was to explore the prevalence of cancer and other disease conditions among farmers and other people who were exposed to chemical pesticides. A community-based epidemiological study was conducted among cardamom farmers and people exposed to the chemical pesticides by using a pre-structured questionnaire containing socio-demographic details, information regarding chemicals, and their disease status. Descriptive and analytical statistics were applied for data analysis. A total of 237 members had interviewed. Among them, 47 were cancer patients, and 169 had comorbidities and other disease conditions. About 54 were suspected of cancer as per symptoms. Among cancers, breast cancer (36.17%) was detected as the major type, and the majority were females (23.3%). The majority of the patients 26 (28.3%) were worked for more than 20 years in the field. The majority of patients with cancer (22.3%) were not taken any of the precaution methods. The frequency of application of the chemicals for most of the patients 14 (33.3%) was more than once in a month. While considering comorbidities, majority were females (76.1%). This study illustrates the high prevalence and risk of cancer and other disease conditions among cardamom farmers and people who are exposed to chemicals in the study location. This data can be correlated with the prevalence of the disease in many other cardamom cultivation areas.

INTRODUCTION: Pesticides are toxic chemicals that destroy pests and weeds in both developed and developing countries ¹. In 1952 India started the production of pesticides BHC near Calcutta. In Asia, India is the second-largest manufacturer of pesticides and have a rank of 12 globally ².

In an agricultural setting, general populations are mainly exposed to pesticides. These chemicals enter into the body through skin, respiratory and digestive routes based on the route. Children also exposed through transplacental route or through breast milk. These all may lead to the accumulation of chemicals that causes major health hazards ³.

There are very limited epidemiological data for the evaluation effect of pesticides on humans. Among the population using pesticides, a small proportion is likely to affect severe effects; however, a huge population may be at risk such as cancer, genetic

<p>QUICK RESPONSE CODE</p> 	<p>DOI: 10.13040/IJPSR.0975-8232.12(5).2884-91</p> <hr/> <p>This article can be accessed online on www.ijpsr.com</p>
<p>DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(5).2884-91</p>	

abnormalities, and reproductive effects, *etc.*^{4, 22} With some short term exposure, they absorbed and eliminated from the body, but in case of long term exposure even small amount they accumulate in the body and can cause severe health effects¹. Pesticides effect depends on the exposure, time of application, precautions to be taken while applying, population, and landscape structure⁴. In some studies shows that increased mortality from pesticides in cardiovascular, respiratory immunologic, neurologic, liver impairment, *etc.* it also related to some psychological effect. Increased cancer mortality was reported in some studies². Certain pesticides affect the hormonal functions of females.

Some of the epidemiological studies show that pesticides can cause menstrual cycle disturbances, abortions, fertility loss, stillbirth, and developmental abnormalities⁵. Certain pesticides are endocrine-disrupting chemicals (EDC) that have the ability to bind estrogens or androgen receptors and cause agonist and antagonist actions⁶. And have the ability to cause breast cancer and other hormonal problems. For example, in the case of thyroid hormones, some pesticides inhibit the production of hormones⁷.

The banned pesticides such as DDT, HCH, *etc.* they still in use both in domestic and agricultural settings⁸. In many areas, farmers face very large problems due to the usage of banned pesticides, incorrect application of pesticides, spraying equipment problems, inappropriate storage of pesticides, and the reuse of pesticide containers for the storage of food and water, *etc.* Some pesticides may be persistent in the atmosphere, and they represent as long-term dangers, and they harm to the food chain^{9, 21}. Besides the effect, in the human body, they distributed in all areas of the environment such as soil, water, air⁸. In air the volatilized pesticides produce vapours and can cause severe damage to other plants and animal species. Pesticides can contaminate water, causes a threat to aquatic life, decreased the level of dissolved oxygen in water⁴.

Pesticide content can found in a variety of food and beverage. Also in cooked food, drinking water, animal feeds, *etc.* Simultaneous exposure to more than one pesticide can cause a lethal synergistic effect^{10, 20}.

MATERIALS AND METHODS:

Study Design and Study Settings: This was a community-based epidemiological study among cardamom workers living in Idukki district, particularly from Udumbanchola taluk. Idukki is a leafy mountainous region in Kerala, 97% of the total area is covered with thick forest. This district is located in the middle part of Kerala. Idukki is known as the spices garden of Kerala. The major cultivation in this area is cardamom, pepper, rubber, vanilla, turmeric, cocoa, *etc.* Most of the region is covered with cardamom plantations. The data were collected from different parts of Idukki district, mainly Udumbanchola taluk, Devikolam taluk, Peerumedu taluk, for a total duration of 6 months during the period of June 2019 to December 2019.

Ethics, Privacy, and Confidentiality: Institutional Human Ethical Committee of Nirmala College of Pharmacy, Muvattupuzha, have assessed the study protocol and given the clearance (No. 016/IHEC/10/2019/NCP) with the instruction to submit the consent form collected before the interview for the data collection. Before the beginning of the interview, the purpose of the study was well taught to the participants. Based on the questions, the responses obtained were recorded. The researchers have assured that all provided information would use only for study purposes with strict confidentiality.

Subject Recruitment and Study Participants: All farmers working in cardamom plantations and the peoples who live within the area of the plantation were included in the study. The farmers outside the district were excluded from the study. G* Power version 3.1.9.2 was used to estimate sample size with the assumption of 95% confidence interval, 5% of estimated error.

Random sampling was used to recruit the subjects. The survey was conducted in the selected areas of the region by face-to-face interview. An average of 30 min was taken to complete the interview by using the questionnaire form. The participants were interviewed only once and completed within 6 months.

Survey Questionnaire & Data Collection: The validated questionnaire was used for data collection

with the clearance of the Ethical Committee (No. 016/IHEC/10/2019/NCP) of our institution. The questionnaire was prepared in English and explained in vernacular language (Malayalam). To identify whether the subjects are feeling any discomfort in understanding of any of the questions, a pilot study was conducted. Before starting the data collection, some modifications were made in the questionnaire form. The questionnaire mainly includes 3 parts, socio-demographic status, information about chemicals, information regarding disease status. Socio-demographic informations include age, gender, education status, family members, major cultivation, plantation areas, and years of working.

Informations type of chemicals using, amount of chemicals, timing of application, informations regarding water resources, frequency of application of chemicals in plantation, whether they are taking any precautions and informations about the money they are spending in each month. Details regarding if they have any disease conditions, about their hospital visit and their medications also were collected. Separate questionnaire for the cancer patients were made to know more about the relation of their condition with the pesticide usage in plantation.

Statistical Analysis: The data were analyzed statistically by using SPSS version 24 and G Power

version 3.1.9.2. Collecting data of the entire population is almost always infeasible. Therefore, we use samples of the population to get a point estimate of our parameter of interest. Here collected samples are 237, so we used a re-sampling (Re-sampling is the method that consists of drawing repeated samples from the original data samples) method called Bootstrapping for increasing the sample size. Using the Bootstrapping method 237 samples was re-sampled without replacement over and over again and the analysis were done in 500 bootstrapped samples, it can be quite good approximation for the population parameters. Categorical variables expressed in percentage and frequencies. Pearson's Chi-square test and fishers exact test was used to identify the significant relationship between two variables.

RESULTS: A total of 237 members had interviewed. Among them 47 were cancer patients and 169 had comorbidities and other disease conditions. About 54 were suspected cancer as per symptoms. A total of 237 participants were selected for the study. Among them, 47 were cancer patients. In that 45 (22.7%) were cardamom workers remaining 2 (5.1%) were not. Based on the disease status and physical symptoms observed 54 were suspected for cancer. Among them, 51 (22%) were cardamom workers and 3 (5.5%) were not.

TABLE 1: FREQUENCY OF CANCER AMONG CARDAMOM WORKERS

Variables	Categories	Cancer		Non-cancer n 237		Suspected as per symptoms Frequency (%)	P value ¹
		Frequency	%	Frequency	%		
Cardamom workers	Yes	45	22.7	153	77.3	51 (94)	0.009
	No	2	5.1	37	94.9	3 (5.5)	

TABLE 2: CLASSIFICATION OF DIFFERENT CANCERS IN CANCER POSITIVE FARMERS (N 47)

Cancer Site	n =47	
	Cardamom Farmers	Others
	% (freq.)	% (freq.)
Breast cancer	36.17(17)	1(2.1)
Brain tumor	8.51 (4)	0
GI cancer	10.64 (5)	0
Lung cancer	8.51 (4)	1(2.1)
Ovarian cancer	8.51(4)	0
Others	23.40 (11)	0
Total	95.74 (45)	4.2(2)

Fisher's exact test has been applied to test the association between the variable. The hypothesis has been accepted if $p < 0.05$ and rejected if it is

$p > 0.05$. Here P-value is $0.009 < 0.05$, so we reject the null hypothesis. That is, there is an association between cardamom workers and cancer.

From the total cancer patients, 18 were diagnosed with breast cancer. In that 17 (36.17%) were cardamom workers, and 1 (2.1%) were not. Within the cardamom workers 5 (10.64%) were GI cancer and 4 (8.51%) were lung cancer, ovarian cancer and brain tumor. 1 (2.1%) diagnosed with lung cancer were not working in the cardamom. Some other type of cancers also identified includes mouth cancer, skin cancer, bone cancer, blood cancer within the cardamom workers.

TABLE 3: SOCIO-DEMOGRAPHIC PROFILE OF CARDAMOM WORKERS (N=237)

Variables	Categories	Cancer	Non-cancer	Total	P value ^{2,1}
		% (Freq.)	%(Freq)	Frequency	
Age	<40	36.8 (7)	63.2 (12)	19	0.131
	40-60	17.4 (23)	82.8 (111)	134	
	>60	20.2 (17)	79.8 (67)	84	
Sex	Male	12.8 (10)	87.2 (68)	78	0.356
	Female	23.3 (37)	76.7 (122)	159	
Years of working in cardamom	<10	12.8 (5)	87.2 (34)	39	0.033
	10-20	15.1 (16)	84.9 (90)	106	
	>20	28.3 (26)	71.7(66)	92	
Precautions taken	Yes	7.5 (3)	92.5 (37)	40	0.032
	No	22.3 (44)	77.7 (153)	197	
Frequency of chemical use	Once in month	18.2 (29)	81.8 (130)	159	0.043
	More than once in month	33.3 (14)	66.7 (28)	42	
	Once in two months	11.1 (3)	88.9 (24)	27	
Amount of chemical uses	1l	11.8 (9)	88.2 (67)	76	0.000
	2l	12.7 (8)	87.3 (55)	63	
	3l	17.3 (9)	82.7 (43)	52	
	4l	54.3 (19)	45.7 (16)	35	

In a total of 237 participants, a major proportion (23) of the study participants with cancer was included in the age category of 40-60 (17.4%). Most of the participants were females 37 (23.3%) who presented with the condition. The majority of the patients 26 (28.3%) were worked more than 20 years in the field and most of them are still remaining in the plantation. While spraying the

chemicals, a major population 44 (22.3%) were not taken any of the precaution methods. The frequency of application of the chemicals for most of the patients 14 (33.3%) was more than once a month. The majority of farmers with the condition 19 (54.3%) were using 4 litres of chemicals for each time.

TABLE 4: SOCIO-DEMOGRAPHIC PROFILE OF THE CARDAMOM FARMERS WITH EXISTING CO-MORBIDITIES AND OTHER DISEASE CONDITIONS (N 237)

Variables	Categories	Present	Absent	Total	P value ^{2,1}
		% (freq)	% (freq)		
Age	<40	42.1 (8)	57.9 (11)	19	0.013
	40-60	73.1 (98)	26.9 (36)	134	
	>60	75.0 (63)	25.0 (21)	84	
Sex	Male	71.8 (56)	28.2 (22)	78	0.526
	Female	76.1 (121)	23.9 (38)	159	
Years of working in Cardamom	<10	51.3 (20)	48.7 (19)	39	0.001
	10-20	82.1 (87)	17.9 (19)	106	
	>20	76.1 (70)	23.9 (22)	92	
Precautions taken	Yes	67.5 (27)	32.5 (13)	40	0.318
	No	76.1 (150)	23.9 (47)	197	
Frequency of chemical use	Once in month	79.9 (12)	20.1 (32)	159	0.001
	More than once in month	54.9 (28)	45.1 (23)	51	
	Once in two months	81.5 (22)	18.5 (5)	27	
Amount of chemicals	1l	67.1 (51)	32.9 (25)	76	0.006
	2l	88.9 (56)	11.1 (7)	63	
	3l	86.5 (45)	13.5 (7)	52	
	4l	65.6 (21)	34.4 (11)	32	
Timing of chemical application	Morning	76.8 (169)	23.2 (51)	220	0.341
	Afternoon	100 (6)	0.0 (0)	6	
Water resource	Near plantation	80.0 (12)	20.0 (3)	15	1.00
	Within plantation	77.3 (163)	22.7 (48)	211	

Association between cancer and socio-demographic profile of cardamom workers was studied by using chi-square test and fisher's exact test. The

hypothesis has been accepted if $p < 0.05$ and rejected if it is $p > 0.05$. Statistically, a significant association was obtained between cancer and years of working

where the P-value is 0.033, precautions taken ($p=0.032$), frequency of chemical use ($p=0.043$), and amount of chemical using ($p=0.000$). No association was obtained between cancer and age ($p=0.131$) and sex ($p=0.356$).

From the total participants, 169 had co-morbidities and other disease conditions. While considering the age most of the participants, 98 (73.1%) were in the age group 40-60. Female participants 121 (76.1%) shows increased level of co-morbidities and other disease conditions when compared to males. There was about 87(82.1%) number of participants who worked over 10-20 years and they showed increased co-morbidities than others. The participants who were not taken any precautions 150 (76.1%) shows more conditions than those taken precautions. Those who use chemicals more than once within a month show a higher rate 28 (54.9%). The participants with an increased level of

co-morbidities and other disease conditions use 2 liters of chemicals per each use. Farmers apply chemicals in the morning shows more than 169 (76.8%) as compared to the afternoon. Those with water resource within the area shows higher rate 163 (77.3) than others.

To identify the association between co-morbidities and other disease conditions with socio-economic status, the chi-square test and fisher's exact test were used. Statistically, a significant association was obtained between co-morbidities and other disease conditions with age ($p=0.013$), years of working ($p=0.001$), frequency of chemical application (0.001), and amount of chemicals used ($p=0.006$). But the test does not show any association with precautions taken ($p=0.318$), sex ($p=0.526$), the timing of application ($p=0.341$), and water resources ($p=1.00$) with comorbidities and other disease conditions.

TABLE 5: PHYSICAL SYMPTOMS PRESENTED BY CARDAMOM FARMERS USING DIFFERENT CHEMICALS

	P value			
	Years in this field	Frequency of chemical use	Timing of application	Sex
Eye redness	0.280	0.718	0.541	0.076
Itching of eyes	0.368	0.382	0.251	0.233
Bulging of eyes	0.55	0.117	0.372	0.026
Watery eyes	0.009	0.544	0.759	0.140
Skin rashes	0.604	0.718	0.418	0.480
Skin discoloration	0.095	0.133	0.338	0.606
Peeling of skin in hands and foot	0.242	0.029	0.795	0.408
Lips discoloration	0.074	0.120	1.000	0.408
Others	0.112	0.238	0.128	0.623

From the total participants' majority of them showed different physical symptoms such as eye redness, itching eyes, bulging of eyes, watery eyes, skin rashes, skin discoloration, peeling of skin in hands and foot, lip discoloration, and some other symptoms such as depression, hair loss, nail yellowing, *etc.*

Chi-square test was applied to find the association between physical symptoms and different variables such as frequency of chemical use, years of working, sex, and timing of application. We reject the null hypothesis if the p-value is less than 0.05. The test shows an association between peeling of skin ($p=0.029$) and frequency of chemical use, watery eyes ($p=0.009$) and years of working, bulging of eyes ($p=0.026$), and sex. And there is no association between other symptoms with the frequency of chemical use, the timing of application, sex, and years of working.

DISCUSSION: Relation with exposure to pesticides in agriculture, forestry, manufacturers, and other sectors and cancer has been studied extensively. Many studies show an elevated risk of cancer due to some occupational exposure among farmers¹¹. The current study aimed to show the association between various variables and different types of cancers and other comorbidities among cardamom farmers using various pesticides.

The prevalence of cancer in the current study was about 22.7% among cardamom workers. The study conducted by Blair *et al.*, in 1995 shows that the elevated rate of some type of cancers in farmers using pesticides¹². Won jin *et al.*, conducted a study in Korea among farmers and identified that the farmers using various chemicals has the risk of increased mortality due to various types of cancers¹³. Based on the observations, this study showed an association between cancer and farmers using

chemicals. The current study was conducted in Idukki, a district of Kerala. Idukki mainly consists of cardamom hills as the largest producer of cardamom in India. The use of various chemical pesticides is increasing day by day to improve productivity. The overuses of chemicals are mainly due to the import of banned pesticides (mainly Organochlorine) to the district from nearby states at a cheap cost. The chemical exposure through various routes, including inhalational, dermal, oral, etc., can lead to various health hazards, mainly cancer. Pesticide residues present in the environment are also a risk factor for the development of cancer. Therefore it is not surprising that the prevalence of cancer in Idukki is high.

In the study prevalence of breast cancer was high among cardamom workers (36.17%). The result of the study shows similarities with the study conducted by Suzanne M. Snedeker in USA¹⁴. Although several studies identified a strong association between chemical pesticides, especially Organochlorine, with breast cancer. Xiaohui et al.; studied the association of serum concentration pesticides with breast cancer¹⁵. In contrast, a meta-analysis by Blair and colleagues concluded that lip cancer as the major type of cancer among farmers¹⁶. This is mainly due to the estrogenic effect of some pesticides; certain pesticides have endocrine-disrupting properties. The obesity-associated with breast cancer shows the effect of pesticides to modify the body mass increases the risk.

The prevalence of cancer higher among females (23.3%) working in the field that was consistent with the study conducted by Dr Pukkala in Finland¹⁷. Females get easily influenced by environmental and other changing conditions. Most of the pesticides are organophosphates; the main mechanism of action is the inhibition of acetylcholinesterase activity. This results in the action of nicotinic receptors, many cellular mechanisms, oxidative stress, and immunotoxicity.

Here it is proven that the chemicals have an effect on female hormones and reproduction. Majority of cancer identified within the age group of 40-60. This is mainly because almost all participants in this age group were active workers. They closely associate with the plantation as well as chemicals.

The persons with long-term exposure to the pesticides are associated with an increased risk of cancer. In this study, the number reported higher those in the field more than 20 years (frequency=26). The long-term exposure leads to the accumulation of toxic chemicals leads to some mutagenic effect leads to cancer. Some of the pesticides are banned due to the mutagenic effect; the overuse of these types of banned pesticides associated with an increased risk of developing cancer. Increased exposure may result from many neurological symptoms. In the survey, it was identified that the majority of farmers (freq. =197) in the field were not taking any precautions like covering the face, masks, protective clothes, etc. This allows the chemicals to enter the body without any barrier. The majority of the farmers with cancer uses chemicals once a month (freq. =29). Whereas the result of a study conducted by Carbonell *et al.*, in 1993 shows increased risk when the frequency increases¹⁸. The study identified the relationship between the amount of chemicals used and cancer. More amount of chemical use leads to cancer (54.3%).

The study also considers other conditions like respiratory, cardiovascular, neurological, dermal, and other psychological conditions. Most of the farmers presented with more than one comorbid conditions. About 73.1% were in the age group of 40-60, and 76.1% were females. The study also considers other co-morbid conditions like cardiovascular, neurological, dermal, and other psychological conditions. This study shows a high prevalence rate for respiratory diseases, arthritis, cardiovascular diseases, and other neurological manifestations. A similar result is seen in a study conducted by Robert *et al.*; in US¹⁹. Respiratory illness was the most prominent condition among cardamom farmers due to exposure to chemical pesticides. These lead to a variety of respiratory disorders such as bronchitis, asthma, and organic dust toxic syndrome. The result of this study shows similarity to the result obtained in a study conducted by Won jin *et al.*¹³ The study has observed some of the physical conditions in workers who were exposed to chemicals are bulging of eyes, watery eyes, itching, and other dermal problems. Most of the workers presented with complaints of peeling of skin while exposed to

these chemicals. Years of working, frequency of chemical use and sex were the variables associated.

Mental health is an important health issue in cardamom workers. Cardamom workers suffer from chronic illness, economic factors. Some of these lead to stress-related disorders such as depression and suicide^{20, 21}. Lack of good quality health care services is the major cause of mortality in the district. The majority of them had some disease conditions but were not yet diagnosed or treated because of the lower economic background. Those taking treatments depend on the hospital outside the district; this creates an additional burden and leads to non-adherence to the treatment. Lack of awareness about the risk of these chemicals and the preventive measures also a leading cause of increased diseases. Conducting medical camps and awareness programs will help to improve the quality of life in area²². The high risk of suicide among farmers has been reported from many studies¹³, where 2000 deaths per were reported from farmers in Korea. In the study, depression is the common factor observed in the majority of workers. Many depressive disorders were reported from the study area. The present study had a limitation that the data about the suicides and other psychological conditions were incomplete. Many Suicidal cases also were reported. This shows the effect of these chemical pesticides on the psychological aspect. In our analysis, many skin diseases were reported. This was mainly due to the contact of chemicals with skin while working in the field.

CONCLUSION: The main aim of the study was to find out the active or passive cases of cancer or any other associative ailments and the association between cancer and other disease conditions because of the pesticides used in the cardamom plantation. It is identified through the present study that a significant association exists between pesticides and cancer. Breast cancer was the major type of cancer identified. The study finds out different variables that associate with the incidence of cancer. Besides cancer, other disease conditions, mainly respiratory diseases, cardiovascular and other chronic conditions, also were reported. Symptoms like skin diseases, psychological diseases, and complications in the eyes were detected through the study. The chemical pesticides

have an impact on surrounding environments as well. Major causes of the psychological problem are associated with the suffering and the economic burden due to the diseases. Lack of medical facilities is the major problem for increased mortality rate due to the delayed treatment and inconsistent follow-ups. More than half of the patients have not been taken any follow-up for their condition because of the lower economic status.

The study reveals the improper health care system in the district and the lack of awareness are the major contributing factors for these occupational ailments.

ACKNOWLEDGEMENT: The authors are thankful to the villagers of the Idukki district and the health care workers of different Panchayat of the district. The authors are also thankful to the Principal and management of Nirmala College of Pharmacy, Muvattupuzha, for the required permissions to collect the data.

CONFLICTS OF INTEREST: Authors declare that there is no conflict of interest.

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How to cite this article:

Mishra B and Johnson D: The impact of carcinogenic chemical use among cardamom farmers and the prevalence of cancer in Idukki district, Kerala. *Int J Pharm Sci & Res* 2021; 12(5): 2884-91. doi: 10.13040/IJPSR.0975-8232.12(5).2884-91.

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