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Unvealing The Potential Health Implications and Carcinogenic Risks Associated with Mosquito Repellents: A Systematic Review

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ABSTRACT

Background: Cancer is a pervasive global health issue, impacting individuals from "all walks of life and global settings". Its complex aetiology encompasses genetic predispositions, environmental carcinogens, and lifestyle factors, mosquito repellents are an add on to one of the aetiological factors of cancer in this era, underscoring the need for multifaceted prevention and treatment approaches. Aim: The purpose of this systematic review explores the carcinogenic potential of mosquito repellents including the major role of DEET(N,N- diethyl-meta-toluamide) exposure and other active ingredients which combines to cause carcinogenic effect on people in various countries causing multiple health issues and systemic diseases both acute and chronic conditions (respiratory disease, disease related to cardiovascular conditions deformities in foetus). Materials and method: PICO and PRISMA analysis were done. A total of four articles were included for the study based on inclusion and exclusion criteria, to better understand the underlying mechanisms in mosquito repellents through different case control study and samples from affected and not affected individuals. Results: The results of this systematic review indicates that exposure to mosquito coil emissions may contribute to the development of multiple types of malignancies. Conclusion: Mosquito repellents, though used for protection against vector-borne diseases, may contain carcinogenic agents that pose potential health risks. Further research is essential to determine their long-term safety and toxicological effects on humans.

Keywords: Mosquito repellents, cancer, organochlorine, DEET.

INTRODUCTION

Cancer incidence is increasingly prevalent amidst the burgeoning global demographic over the past few decades< with an estimated range of 19.3 million new cases and 10 million cancer-related deaths in 2023 alone.1 In 1996, WHO report estimated the worldwide annual consumption of mosquito coils to be ~29 billion pieces. Major active ingredients of mosquito coil are organochlorine compounds and pyrethroid (meperfluthrin/cypermethrin/pynamin/ES Esbiothrin), formaldehyde, picaridin (KBR 3023), permethrin IR3535 (3-[N-butyl-N-acetyl]-amino propionic acid) oil of lemon eucalyptus (OLE), citronella catnip oil, prallethrin and pyrethrin-0.3%-0.5% of coil mass other components of mosquito repellents include organophosphorus (trichlorfon/chlorpyrifos), carbamate (propoxur/ di methiocarb)t5, There are few specific components which has high carcinogenic potency: DEET(N,N diethyl-meta-toluamide), Chlorpyrifos,Propoxur,Organochlorine,compounds(DDTdichlorodiphenyltrichloroethane),Lindane(Gamma-Hexachlorocyclohexane)Chlordane.2

While newer mosquito repellents opt for alternative active ingredients, such as pyrethroids, organophosphate, and insect growth regulators (IGRs), to minimize the use of known carcinogens, research suggests that specific components, including the organophosphate Malathion and the IGR pyriproxyfen, continue to pose cancer risks. Herbal mosquito repellents contain Azadirachta indica (Neem) seed hexane extract. Mosquito repellents are of varies types which involves Coil, Cream, Mosquito Sprays, Roll-On, Cream, Net, Spray, Dispenser Devices.

When a mosquito coil is burnt the insecticides evaporates with smoke, which immobilizes the mosquito

and prevents entry. The combustion of remaining materials generates large amount of submicrometric particles and gaseous pollutants. The submicrometric particles may reach the lower respiratory tract and be coated with a wide range of organic compounds such as polycyclic aromatic hydrocarbons.1The combustion of a single mosquito coil emits an equivalent amount of fine particulate matter (PM 2.5) as the combustion of 75-137 cigarettes.4

Longtime exposure to MCS (Mosquito Coil Smoke) induce asthma and persistent wheeze in children.1 Mosquito repellent incenses area type of mosquito repellent that uses smoke or vapour to repel mosquitos.1 Fumigation of mosquito repellents incenses releases harmful fine particles and gases posing serious health risks. Prolonged exposure is of more risk causing Respiratory issue like asthma Inflammation and Oxidative stress, Neurological damage, DNA mutations, increased cancer risk. The deposition of aerosol particles size, lung anatomy and breathing patterns.2 Mechanism of mosquito repellent incenses changes the particle composition and results in variations in the breathing behaviour and airflow patterns within the lung.2 Liquid electric mosquito repellents, also known as liquid vaporizers or electric mosquito killers, have gained significant popularity in recent years.19

Some mosquito repellents are combined with sunscreen and used. These products are crucial for travellers and people engaged in outdoor activities. This increases the skin cancer risks.2 Using capillary technology, liquid electric mosquito repellent devices heat and steadily release insecticides, providing a consistent mosquito-repelling effect that lasts around 60 days.3 Recognizing all these risk factors, about 70% of females who develop breast cancer do not have identifiable risk factors.5 Co-administration of a synthetic insect repellent like DEET together with chemical substance such as oxybenzone is suspected to increase absorption of all topically applied mosquito repellents and leads to health risk. 6 Usage of DEET (active component) can also cause Retinoblastoma- a malignancy which occurs due to absence of both the copies of RB1 gene that normally suppresses retinoblastoma. Commonly observed in retinal cells of embryos, babies and young children.23
In addition to the active components of mosquito repellents, there are 16 Volatile Organic Compounds which are released from all three types of mosquito repellents including coil, mat, liquid which increases the health risks among human populations. Thus, this systematic review aims to unveil the potential health implications and carcinogenic risks associated with mosquito repellents.

MATERIALS AND METHODS:

This systematic review was conducted for unveiling the carcinogenic potential of mosquito repellents including the major role of DEET exposure and other active ingredients which combines to cause carcinogenic effect on people in various countries causing multiple health issues and systemic diseases both acute and chronic conditions (respiratory disease, disease related to cardiovascular conditions deformities in foetus). This Systematic review was conducted following PRISMA Guidelines24.

ELIGIBILITY CRITERIA

Inclusion criteria

- This study includes randomised control trial that has been done in between 2000-2023
- It consists of full-length text articles from web engine such as pub-med, google scholar, science direct and research gate.
- It elaborates the articles on carcinogenic potential of mosquito repellents.

Exclusion criteria

- Studies consisting of full-length articles curated in other languages other than English.
- It excludes materials in which components of the mosquito repellents which does not have potential carcinogenic effect on humans.

SEARCH STRATEGY

Articles were collected from databases such as PubMed, Cochrane, Google Scholar, and Embase. Search term used for identification of the studies were "Mosquito Repellents" AND "Cancer Potential"; " Mosquito Repellents " AND "health hazards".

STUDY SELECTION:

This research resulted in 200 articles from which 20 were full length articles having accessibility and are eligible for review. Finally,4 articles were selected for this systematic review.

RESULTS:

This research resulted in 56 articles, of which 20 were full text articles having accessibility and were eligible for review. Ultimately, four articles were chosen for inclusion in this systematic review [Figure 1].

Figure 1: Flow chart showing the number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review.

PRISMA FLOWCHART

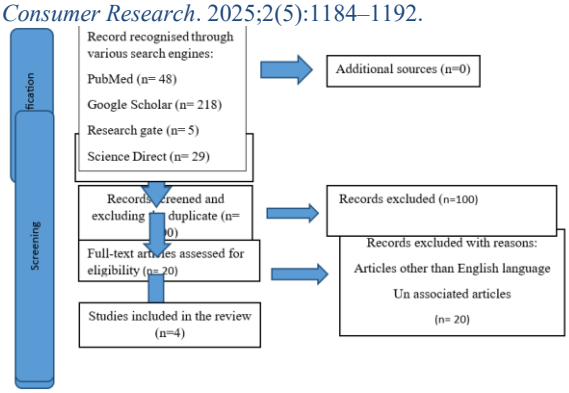


Figure 1 shows the number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review.

Table 1: Characteristics of the study.

S.no	Author name	Year	Sample size	Study design	Patient characteristics	Duration	Patient Allocation
1.	Shu-Chen Chen et. al[1]	2007	147	Hospital based case-control study	Questionnaires were administered to 147 primary lung cancer patients to ascertain demographic data, occupation, lifestyle data, indoor environmental exposures.	1.5 months	Group 1: patients agreed to participate (n=147) Group 2: patients not able to participate (n=1)
2	Sebelework Mekonnen et.al[2]	2021	100	A case-control study	A case-control study design was employed among breast cancer patients and non-breast cancer individuals (18 to 55 + years age groups)	2 months	Group 1: serum separation, extraction and cleanup using standard analytical procedure among breast cancer patients(n=50) Group 2: serum separation, extraction and cleanup using standard analytical procedures among non-breast cancer patients(n=50)
3	Lina Wang 1* et. al[3]	2017	10	Randomised control trial	Chamber experiment to characterize major pollutants from three types of mosquito repellent incenses.	1 month	Group1: experiment was performed in three distinct ages (age 21 months) Group 2: experiment was performed in three distinct age (age 8 years) Group 3: experiment was performed in three distinct age (age 21 years)
4	Xiaohui Xu et.al[4]	1999-2000.	1,475. 1,693.	Cross sectional study	blood samples from the one-third of the participants ≥ 12 years of age were collected and measured for serum CONC of several OC pesticides or their metabolites	3 years	Group 1: blood samples were collected and measured for serum OC CONC(n=1,475) Group 2: blood samples were collected and measured for serum OC CONC(n=1,693) Group 3: blood samples were collected and measured for serum OC CONC (n=1,585)

		2001-20002200303-20044.	1,585.				

Table 1 shows the Characteristics of the studies included in the systematic review with Author name, samples recruited, sample characteristics, duration of the study and sample allocation.

Table 2: Characteristics of the primary outcome and results of the studies included in the systematic review.

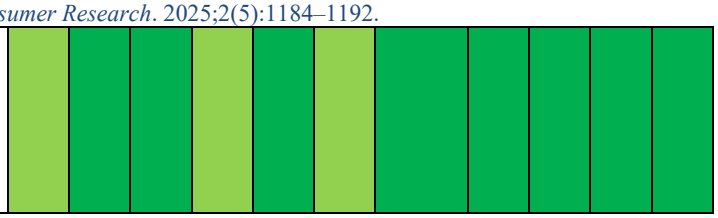
S.no	Author name	Year	Effect measure	Result	Conclusion
1	Shu-Chen Chen et. al[1]	2007	a multiple unconditional logistic model was employed to obtain the adjusted odds ratio (OR) and 95% confidence interval (CI) for selected variables.	Of the 147 patients with histologically confirmed primary lung cancer, 91 (61.9%) had adenocarcinoma and 30 (20.4%) squamous cell carcinoma.	This study highlights the potential carcinogenic effects of mosquito coil smoke suggesting a link between exposure and increased risk of lung cancer
2	SebleworkMekonen et.al[2]	2021	A total of 100 blood samples were collected using a voluntary based convenient sampling technique. The extraction and clean-up of the serum samples were done using analytical methods.	From all of the OCPs detected in human blood serum, heptachlor is observed with higher mean concentration in cases (6.90±4.37 µg/L) and controls (9.15±3.84 µg/L).	This study reveals the presence of banned OCPs and their metabolites in the serum of Ethiopian participants highlighting the carcinogenic effects.
3	Lina Wang1* et. al[3]	2017	The measurement was conducted in a large-scale chamber,	Results showed that the total deposition fraction of emissions from the three 383	This study found that typical mosquito repellents incenses emit significantly high concentrations of pollutants emphasizing the need for comprehensive

			which was designed for online and offline measurement of pollutant emissions or to validate mathematical models for specific pollutant sources.	types of mosquito repellent incenses was 19.8, 22.4% and 19.0%, respectively.	characterization of pollutant emissions and their implications for human health risk assessments.
4	Xiaohui Xu et.al[4]	1999-2000 2001-2002 2003-2004	Blood samples were collected, allowed to clot and then serum - separated and frozen. A standardized analytical protocol was employed, featuring quality control samples.	The sample of 4,237 participants included 4,109 individuals without cancer and 128 cancer cases including 63 breast cancer cases and 65 prostate cancer cases.	Our research suggests that exposure to organochlorine pesticides may be associated with an increased risk of prostate and breast cancers, these findings have significant implications for public health and emphasize the need for targeted interventions to reduce OC pesticide exposure and prevent hormone-dependent cancers.

Table 2 shows the intervention used in the study included with the outcome.

Table 3: Bias analysis as included in the studies

Author name	Randomization	Allocation Concealment	Comparison group	Confounding	Experimental conditions	Blinding	Complete outcome data	Exposure Characterization	Outcome Assessment	Outcome Reporting	No other threats
Shu-Chen Chen et al., 2007 (lung cancer vs mosquito coil smoke)											
Seblework Mekonen et al., 2021 (OCPs & breast cancer, Ethiopia)											
Lina Wang et al.,2017 (repellent incense pollutant chamber trial)											

Xiaohui Xu et al.,2010 (serum organochlorines & cancers, NHANES USA)	

Definitely low risk of bias
Probably low risk of bias
Probably high risk of bias
Definitely high risk of bias

Table 3 Shows the risk of bias in all the included studies based on the Office of Health Assessment and Translation assessment tool.[25,26] Dark Green colour indicates Low Risk for adequate methods and transparency bias unlikely to affect the results. Light Green colour indicates some concerns for uncertainty about risk of bias due to imcomplete reporting. Red colour indicated high risk for clear flaws in design or reporting that may significantly affect the results.

DISCUSSION:

This Systematic Review confirms that exposure to mosquito coil emissions may contribute to the development of multiple types of malignancies. Organochlorine compounds and pyrethroid, (meperfluthrin/cypermethrin/pynamin/ES Esbiothrin , transfluthrin) formaldehyde, picaridin (KBR 3023), permethrin IR3535 (3-[N-butyl-N-acetyl]-amino propionic acid) oil of lemon eucalyptus (OLE), citronella, catnip oil, prallethrin and pyrethrin 0.3%-0.5% of coil mass, oct-chlro-i-propyl ether (S-2,S-421)(active ingredient) can interfere with hormone signalling pathways, by disrupting normal hormone function, potentially leading to carcinogenic outcomes due to their Xeno estrogenic properties.[1,23]As mentioned earlier mosquito coil combustion generates fine particles, PAHs, and formaldehyde, other volatile organic compounds are Benzene, Cyclohexane, Cyclohexane, methyl-D-Limonene, Ethyl acetate, Ethylbenzene, Heptane , Isopropyl benzene ,Methyl isobutyl ketone ,Nonane, Octane, Styrene, Toluene, Xylene, alpha Methyl styrene ,n-Hexane(most frequently detected substance).[1]which can coat the lungs and are associated with increased lung cancer risk in individuals.

Shu-Chen Chen et. al,2007[1] aimed to evaluate the population percentage affected by carcinoma due to mosquito repellents usage. A total of 147 people admitted for the study 1 person failed to participate. Out of 147, 91(61.9%) had adenocarcinoma and 30 (20.4%) squamous cell carcinoma. This study concludes that higher frequency of burning mosquito coils increases risk of lung cancer risk of cigarette smokers. Comparative studies with different formulations and a larger population-based sample could further optimize supportive care and prevention strategies.

Seblework Mekonen et.al, 2021[2] evaluated the characteristics of organochlorine pesticides (OCPs) may contribute to breast cancer and prostate cancer risk due to the presence increased concentration of OCPs in the serum. Analytical studies were performed and 100 blood samples were collected cancer cases using a voluntary based convenient sampling technique. Analysis showed that Heptachlor is observed with higher mean concentration in cases (6.90±4.37 µg/L) and (9.15±3.84 µg/L). Furthermore, studies could focus on elucidating the risk factors of OCP concentration on human serum levels.

Lina Wang1* et. al,2017[3] investigated the major pollutants from different age group people. A largescale chamber was conducted among three types of repellent incenses. The study found that total deposition fractions of emissions from the three types of mosquito repellent incenses was 19.8%, 22.4%, 19.0%.

Xiaohui Xu et.al,1999-2000, 2001-2002, 2003-2004[4] evaluated the efficacy of serum concentration of several OC pesticides and their metabolites. Blood samples were collected and allowed to clot and serum separation was done. A Sample of 4,237 people participated including 4,109 of them are nonaffected and 128 affected participants. They found that out of 128 cancer cases 63 breast cancer cases and 65 prostate cancer cases. On basis of bias assessment exposure to organochlorine pesticides may be associated with an increased risk of breast cancer and prostate cancer, these findings have significant implications for public health and emphasize the need for the targeted interventions to reduce OC pesticides exposure and prevent hormone-dependent cancers.[7,23]

Cancer risk is not only by mosquito coil or incenses which generates smoke but also by electric mat and electric liquid repellents where 16 Volatile Organic Compounds are involved out of which 3 major concentrations are higher than other constituents. [8]Repellents has investigated the connection between workplace exposure to DEET and the incidence of testicular cancer, revealing a potential correlation between high levels of insect repellent exposure and an increased risk of developing other malignancies.[9] Mosquito repellents can trigger various health issues, including respiratory problems, eye and throat irritation, and increased risk of heart diseases and asthma.

Accidental ingestion of liquid mosquito repellents can result in transfluthrin poisoning which manifests as intravascular haemolysis and methemoglobinemia, uncontrolled seizures, and rise in leucocytes counts in

juveniles and adults. Transfluthrin contribute to severe morphological deformities during foetal developing stage and also in a developed child and it accounts for a high mortality rate. Analysis showed that DDT and DDE were present in staple foods, including teff, maize, and red pepper.

Findings shows that expression of RB1 gene as well as Cytokines Block Micro Nucleus (CBMN) assay in cultured human lymphocytes were used the potential mutagenic and genotoxic and cytotoxic effects of DEET.[33] Ingestion of DEET can cause rapid actions like coma, convulsions, respiratory disease, severe hypotension may lead to death. This occurs by both oral or cutaneous route. Seizures is the significant symptom in chronic exposure to DEET. [28] As per studies mosquito repellents affects Red Blood Cells (RBC) White Blood Cell (WBC) and lung damage is confirmed through animal studies.

This systematic review suggests that exposure to mosquito repellents, organochlorine pesticides, DEET, other organochlorine compounds would culminate in chronic systemic conditions which gradually may lead to malignancies. These components cause damage to not only adults also affect the foetus through placental transmission. Major vital organs are viable to malignancies based on the extent of exposure to such components.

Various studies show results of hormone related malignancies, some common examples are breast cancer and prostate cancer as evaluated by Xiaohui Xu et.al[4] and incenses type of repellents has become the need of day-to-day existence, respiratory diseases are the result of using incense repellents which leads to lung cancer. Some formulations of mosquito repellents are available with the combination of repellent and sunscreen, this combination is more prone to skin cancer(melanoma) affecting the teenage group of people along with allergic reactions and other skin disease which is highly transmittable to other people. Mosquito repellents show alterations in the leukocyte profile and histopathology of lung in case of carcinoma involving lung and associated structures. One of the prevalent types of carcinomas is Retinoblastoma affecting young age people.

CONCLUSION:

Despite being widely used to protect against vector-borne diseases, mosquito repellents can be harmful to one's health because some of their active ingredients are toxic and carcinogenic. Significant negative effects are currently highlighted by the evidence, but there is not enough conclusive data to draw firm conclusions about causal relationships. To clarify the long-term effects of mosquito repellent exposure on human health, comprehensive longitudinal studies, toxicological analyses, and clinical trials are therefore necessary. The possible health risks connected to these widely used products can be reduced by enforcing strict regulations, encouraging the use of safer natural substitutes, and raising public awareness.

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