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The Inglorious Link Between Cancer and Agrochemicals a Systematic Review.

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ABSTRACT

Due to the increase in the world's population. The need for increase crop yield is on the rise; farmers answer to this involves the use of fertilizers and pesticides. These agrochemicals have been implicated in some diseases involving the deadly Cancer. Five databases were searched using the key words cancer and fertilizer, pesticides. The databases that were searched include: Google Scholar, Pubmed, Hinari and semantic scholar. About 14 articles were selected, within a five year span of 2014 -2019 using keywords as cancer, fertilizer and pesticides. Little is known on the link between cancer and these agrochemicals. Hence, the goal of this study.

Keywords: Cancer, Fertilizer, Breast Cancer, Health, Pesticides

1. INTRODUCTION

Cancer is the abnormal growth of cells anywhere in the body .i.e. they penetrate the normal body tissues. These cells are also called malignant or tumor cells (Davis *et al.*, 2019). A tumor is any abnormal penetration of cells, which can either be benign or malignant. A Benign tumor e.g. Common skin wart is when the growth remains confined to its original location and it is neither invading the surrounding normal tissue nor spreading to distant body sites. A Malignant tumor, on the other hand, is capable of both invading the surrounding normal tissue and spreading throughout the body with the help of the circulatory or lymphatic systems (Cooper, 2000).

Only Malignant tumors are properly referred to as cancers, because of their ability to move from one site to another in the body. This characteristic makes cancer so dangerous (Cooper, 2000). According to World Health Organization (2019), the word Cancer is used as a generic term for a "group of disease" that affects any part of the body because of the rapid creation of cells that grow beyond their usual boundaries and can then invade adjoining parts of the body and spread to other organs in the body. These abnormal growing cells can move through the blood and lymph systems to other organs where they continue their uncontrolled growth cycle. This process is termed Metastasis (Davis *et al.*, 2019).

In the year 2018, Cancer was discovered as the second leading cause of death globally and is responsible for an estimated 9.6 million deaths. I.e. In the whole world, about 1 in 6 deaths is caused by cancer (WHO, 2019). There are over 200 types of cancer but; Prostrate, Lung, Bladder, Colorectal, Endometrial, Kidney, Melanoma, Pancreatic, Thyroid, Breast, Leukemia, Brain tumor cancers are the most prevailing types.(Davis *et al.*, 2019).

1.2 Global Cancer Burden

Since 2018, the global cancer burden has been estimated to have risen to 18.1 million new cases and 9.6 million deaths. One in 5 men and one in 6 women worldwide develop cancer during their lifetime, one in 8 men and one in 11 women die from the disease. It has also been recorded that worldwide, the total number of people who stay alive within 5 years of a cancer diagnosis (i.e. the 5-year prevalence) is estimated to be 43.8 million. (WHO, 2018). With an estimated 238,000 new cancer cases occurring among adults aged 60 years and older in sub-Saharan Africa in 2012, population ageing in the region will lead to a considerable rise in cancer incidence in the next decades, with an almost three-fold increase in the number of new cancer cases projected by 20,502, even if incidence rates remain stable (Pilleron *et al.*, 2018)

Cancer statistics and epidemiological findings that were accumulated in the past 5 years were to assess the causal involvement of the main carcinogenic agents in different cancer types for the year 2012. And it was brought to the conclusion that infections caused by certain bacteria, fungi, viruses or parasites are some of the risk factors for the specific types of cancers (Plummer *et al.*, 2016). Out of the 14million new cases of cancer, it was found that 15.4% (2.2million) were caused by carcinogenic infections

1.3 Causes of Cancer

Carcinogens are those substances that cause cancer (Cooper, 2000). WHO has classified these carcinogens into 3 groups, which includes;

- Physical carcinogens; Ultraviolet rays from sunlight and ionizing radiation like; Uranium, radon, radiation from alpha, beta, gamma, and X-ray-emitting sources (WHO, 2018; Davis *et al.*, 2019)
- Chemical carcinogens; Asbestos, components of tobacco smoke, Aflatoxin (amycotoxin and also a food contaminant), and Arsenic (a drinking water contaminant), Benzene, Nickel, Cadmium, vinyl chloride, benzidine, N-nitrosamines, etc. (WHO, 2018;Davis*et al.*, 2019)
- Biological carcinogens; like infections from certain viruses, bacteria, or parasites. (WHO, 2019)

Other possible factors or causes are;

- Pathogens like Human papillomavirus (HPV), Epstein-Barr virus (EBV), Hepatitis viruses B and C, Kaposi's sarcoma-associated herpesvirus (KSHV), Merkel cell polyomavirus, *Schistosoma* spp., and *Helicobacter pylori*; other bacteria were being researched as possible agents of causing cancer. (Davis *et al.*, 2019)
- According to the International Agency for research on cancer, red meat (such as beef, lamb, and pork) when been processed either by smoking, salting or cured were classified as a high-risk agent for causing cancer. (Davis *et al.*, 2019).

3. METHODOLOGY

Five databases were searched using the key words cancer and fertilizer, pesticides. The databases that were searched include: Google Scholar, Pubmed, Hinari and semantic scholar. The breakdown is as shown below.

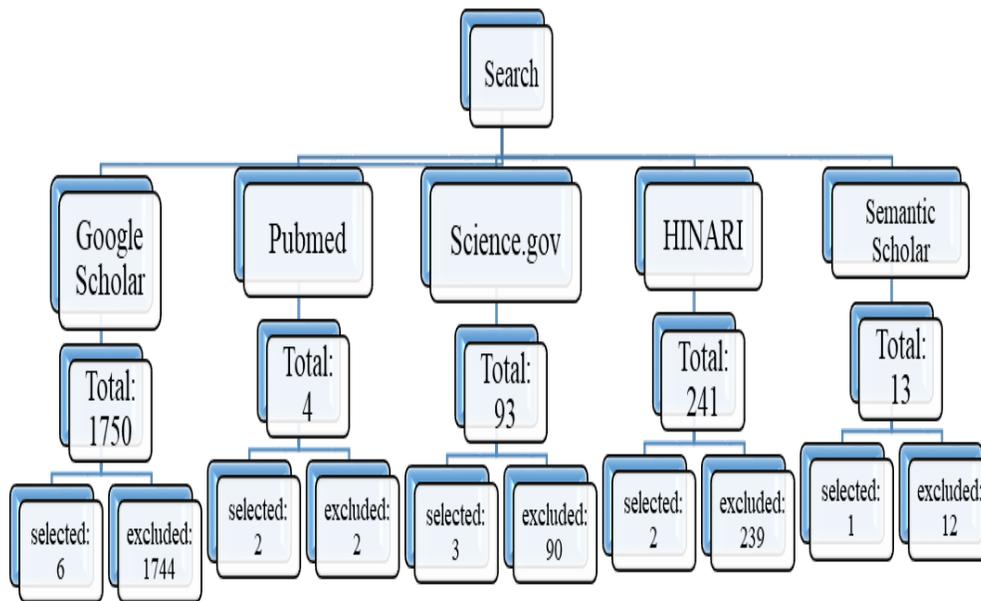


Figure 1: Total articles selected in five different databases for this systematic review

3.1 Fertilizers

Plants need food and some essential elements (Such as; Hydrogen, carbon, and oxygen) for their development and growth. (Staff *et al.*, 2018) These nutrients or elements are gotten either from soil minerals and soil organic matter or by inorganic or organic fertilizers. (Staff *et al.*, 2019)

According to Justus von Liebig's Law of the minimum which states that *"if one of the essential plant nutrients is deficient, plant growth will be poor even when all other essential nutrients are abundant"* there are essential plant nutrients other than nitrogen (N), Phosphorous (P), and Potassium (K) (Macronutrients) that plants require to grow, and these are known as the limited nutrients or Trace elements. (Savoy, 2012; ACG Materials, 2019)

- The Macronutrients are; nitrogen(N), phosphorus (P), potassium (K), calcium (Ca), sulfur (S), magnesium (Mg), carbon (C), oxygen(O), hydrogen (H)
- The Micronutrients (or trace minerals): iron(Fe), boron (B), chlorine (Cl), manganese (Mn), zinc (Zn), copper (Cu), molybdenum (Mo), nickel (Ni) (Staff, 2018)

3.2 Types of Fertilizers

Fertilizer is a substance that is either sprayed or applied directly or indirectly to the crop or soil to improve plant growth and product quality .According to Staff (2018), there are three (3) types of fertilizer; Chemical Fertilizer, Organic Fertilizer, Bio-fertilizer

3.3 Chemical Fertilizers (Synthetic Fertilizer)

This type of fertilizer contains nutrients like nitrogen, phosphorus, and potassium which are made chemically with the aid of influencing plant growth (Staff, 2018). Examples of this fertilizer are; Ammonium nitrogen fertilizer, Nitrate Nitrogen fertilizer, Soluble Phosphate (containing N/P with the ratio of 2:1) and Potassium Chloride (Muriate of Potash)

The Advantages of Chemical Fertilizers

Nutrients are soluble and available to the plants making the effect direct and fast, The price is lower and more competitive than organic fertilizer, They are high in nutrient content; therefore it requires little quantity (Staff, 2018). Disadvantages of Chemical Fertilizers. It increases soil degradation. (I.e. Increment in soil acidity, nutrient imbalance, and low crop yields.), since it is easily soluble in water, it can be lost through leaching or erosion thereby reducing the effect on the crops, Too much application can result in negative effects such as leaching and pollution of water resources, destruction of microorganisms and friendly insects, crop susceptibility to disease attack, acidification or alkalization of the soil or reduction in soil fertility. (Staff, 2018)

3.4 Organic Fertilizers

Also known as Farmyard Manure, it supplies a variety of rich nutrients, elements, organic acid and promotes the growth of microorganisms when applied to the soil (Alliance, 2019).

Organic fertilizers include naturally occurring organic materials like manure, worm castings, compost, seaweed or naturally occurring mineral deposits (Staff, 2018)

3.4.1 Types of Organic Fertilizers

- ❖ **Animal manures:** Animal manure is a complete organic fertilizer that comprises of livestock's waste. This type of fertilizer is tagged as the best type but it can be hazardous when applied without treatment because it may contain Nematode, eggs or microorganisms like *Escherichia coli* (Staff, 2018; Alliance, 2019)
- ❖ **Sewage sludge:** It is a recycled product of municipal sewage treatment plants (Staff, 2018). Processed sludge helps in soil improvement and not just helping plants grow but solving the problem of waste treatment (Alliance, 2019).
- ❖ **Composts:** Compost is made from a variety of raw materials in which the finished products are similar in their final concentrations of nitrogen, phosphorus, and potassium (Staff, 2018).

Advantages of Organic Fertilizers

- ❖ Organic fertilizers are better sources of nutrients in balanced amounts than inorganic fertilizers where the soil is deficient in both macro and micronutrients, It is beneficial because it supplies micronutrients and organic components that increases soil moisture retention and reduce the leaching of nutrients, It can also be used on acid-tolerant and those better suited to neutral or alkaline conditions, Organic fertilizers can improve the soil life and long-term productivity of soil, and may prove a large depository for excess carbon dioxide, Organic nutrients increase the abundance of soil organisms by providing organic matter and micronutrients for organisms such as Mycorrhiza fungi (Staff, 2018)

Disadvantages of Organic Fertilizers

It is hard to get, not sterile and sometimes contains low nutrient content, It is more costly compared to synthetic fertilizer, Organic certification requires documentation and regular inspections, Organic fertilizers still release nutrients into their surroundings; these nutrients can find their way into local streams, rivers, and estuaries just as nutrients from synthetic fertilizers do (Staff, 2018).

3.5 Biofertilizers

Bio-fertilizer (A.K.A Microbial Inoculants) are made from specific microorganisms like bacteria, fungi, and algae that have the capability to fix atmospheric nitrogen and also to convert soluble phosphate and potash into the soil in various forms for the plants (Staff, 2018)

Advantages of Bio-fertilizers

Bio-fertilizers are less costly than Chemical Fertilizers, This type of fertilizer provides not only nitrogen but some growth promoting substances like hormones, vitamins, and amino acids, The use of bio-fertilizers continuously helps in the improvement of the soil structure(Staff, 2018).

3.6 Pesticides

Depletion of soil nutrients, Pests, weeds and diseases suppress Crop yields (Sheahan *et al.*, 2016). Substances used to prevent, kill, or fend off any pest like insects, animals; weeds or even microorganisms are called Pesticides (Grube *et al.*, 2011; Bonner *et al.*, 2017). A definition of Health Risk Assessment was developed by the National Academy of Sciences in 1983 which consists of four parts, (I.e. Hazard Identification, Dose-Response Assessment, Exposure Assessment, and Risk Characterization)

- ❖ **Hazard Identification:** It is a process of determining if human exposure to a pesticide's active ingredient could cause an increase in the incidence of a health condition (e.g., cancer, birth defects, heart disease, immune disorders, and neurological injury) or if exposure to either domestic animals or wild animals might be negatively affected.(National Academy of Sciences 1983; Bonner, 2017)
- ❖ **Dose-Response Assessment:** It is the process of characterizing the relationship between the dose of a specific administered pesticide and the incidence of the health effect in the exposed populations and estimating the effect as a function of the pesticide dose. This process has to do with assessing the intensity of the exposure, duration of the exposure, the personal protective equipment (PPE) used, the age pattern of exposure, and other lifestyle factors that may modify risk. (National Academy of Sciences 1983; Bonner, 2017)
- ❖ **Exposure Assessment:** is the process of measuring the intensity, frequency, and duration of human or animal exposure to a specific pesticide. In population settings, risks as a result of the population are partly a function of the prevalence of exposure (National Academy of Sciences 1983; Bonner, 2017)

3.7 Pesticides and Carcinogens

During the spraying of pesticides, farmers do not use safety masks, gloves and other protective gear which may result in the access of pesticides in the bloodstream through inhalation and skin exposure which can adversely affect their eyes, skin and the respiratory system. It may also affect the human endocrine and immune systems thereby promoting the development of cancer (Bhandari, 2014; Choudhary, 2014; Sharma *et al.*, 2017).

According to International Agency for Research on Cancer, some pesticides have been found to contain probable human carcinogens like Lindane (Group 1 Human carcinogen) and DDT; Dichlorodiphenyltrichloroethane (Group 2 Human carcinogen) which has been shown that they do not only cause immunosuppressive effects on human cells but also increase the oxidative stress in human peripheral blood mononuclear cells leading to proliferation of liver cancer cells and stimulation of human colon cells (International Agency for Research on Cancer, 2017; Bonner *et al.*, 2017).

3.8 Carcinogens associated with Chemical Fertilizer

Due to the basic need of farming, the soil may be polluted by the accumulation of various heavy metals, through emissions by industries, mining process, disposal of high metal wastes, gasoline, application of fertilizers, sewage sludge, pesticides, wastewater irrigation, coal combustion residues, etc. In the past, a large amount of chemicals is annually applied at the agricultural soils as fertilizers and pesticides. These applications may result in the increased level of heavy metals, particularly Cadmium, Lead, and Arsenic in the soil (Atafar *et al.*, 2010; Sharma *et al.*, 2017).

Some nitrosamine compounds are categorized by the International Agency for Research on Cancer (IARC) as probable carcinogens (group 2A) for humans (Xu *et al.*, 2015; Ghaffari *et al.*, 2019). During such findings of the studies, the focus on the association between nitrates intake and various cancers such as the brain, esophagus, stomach and colorectal were unclear (Quijano *et al.*, 2017). However, it is suggested that high levels of nitrate intake from food can be taken into consideration as a key risk factor in the development of certain cancers (Chetty *et al.*, 2017; Ghaffari *et al.*, 2019).

When fertilizers (Chemical Fertilizer) are used in farmlands, they are transmitted directly or indirectly into the corns and vegetable that affects human health. The extreme use of fertilizers may pollute the underground water with nitrate (very harmful to humans or livestock). Nitrate concentrated water can halt some of the hemoglobin in the blood (Miah *et al.*, 2014; Sharma *et al.*, 2017). The release of unused nitrogen from agricultural fields in the form of NO_2 contributes to global warming 298 times more than CO_2 (Signor and Cerri 2013; Hakeem *et al.*, 2016).

The meticulous use of N fertilizers is leading towards a negative impact on the environment in the agricultural production systems (Xu *et al.* 2000; Smil 2002; Zu *et al.* 2002; Killebrew and Wolff 2010). Reports have shown that nitrogenous fertilizer is one of the major sources of NO_3 contamination of groundwater. If this contaminated groundwater is pumped for drinking purpose, it may have a direct upshot on human health leading to either Acute or Chronic toxicity (Hill, 1999; Nolan *et al.*, 2000; Bjorne *et al.*, 2004; Hakeem *et al.*, 2016).

Acute toxicity is articulated when nitrite enters the bloodstream in large quantities and oxidizes the ferrous iron of hemoglobin to the ferric form producing methemoglobin, making transport of oxygen difficult which may lead to results in methemoglobinemia (Fewtrell, 2004; Hakeem *et al.*, 2016). 80% of reports have shown that the total intake of nitrates in human originates from vegetables and some part of drinking water. The quality of drinking water is harmfully affected by nitrate through the possible formations of nitrite in babies causing methemoglobinemia and cancer in older persons due to the formation of nitrosamines in the digestive tract (Ward 2009; Hakeem *et al.*, 2016). Inorganic N applied to the soil can be absorbed by the plants, utilized by microorganisms, subjected to nitrification and denitrification. But their excessive and careless use of this inorganic fertilizer further highlights the environmental degradation besides affecting the quality of crops, human and animal health (Vymazal, 2007; Hakeem *et al.*, 2012; Hakeem *et al.*, 2016).

In surface water, the presence of high nitrogen results in the growth of algae and plants, thus accelerating eutrophication, and as a result affects water quality and usage (EPA 2007; Shen *et al.*, 2011; Hakeem *et al.*, 2016). The reports of incidence of stomach cancer in humans, particularly in infants, and of non-Hodgkin's lymphoma is due to intake of water contaminated with nitrate (Mueller *et al.* 2001; Ikehata *et al.* 2010; Inoue-Choiet *et al.*, 2012; Hakeem *et al.*, 2016). Nitrosamines produced from nitrite are reported to be carcinogenic; and NH_3 gas is a pollutant because of its corrosive nature due to the formation of ammonium salts (Hakeem *et al.*, 2016).

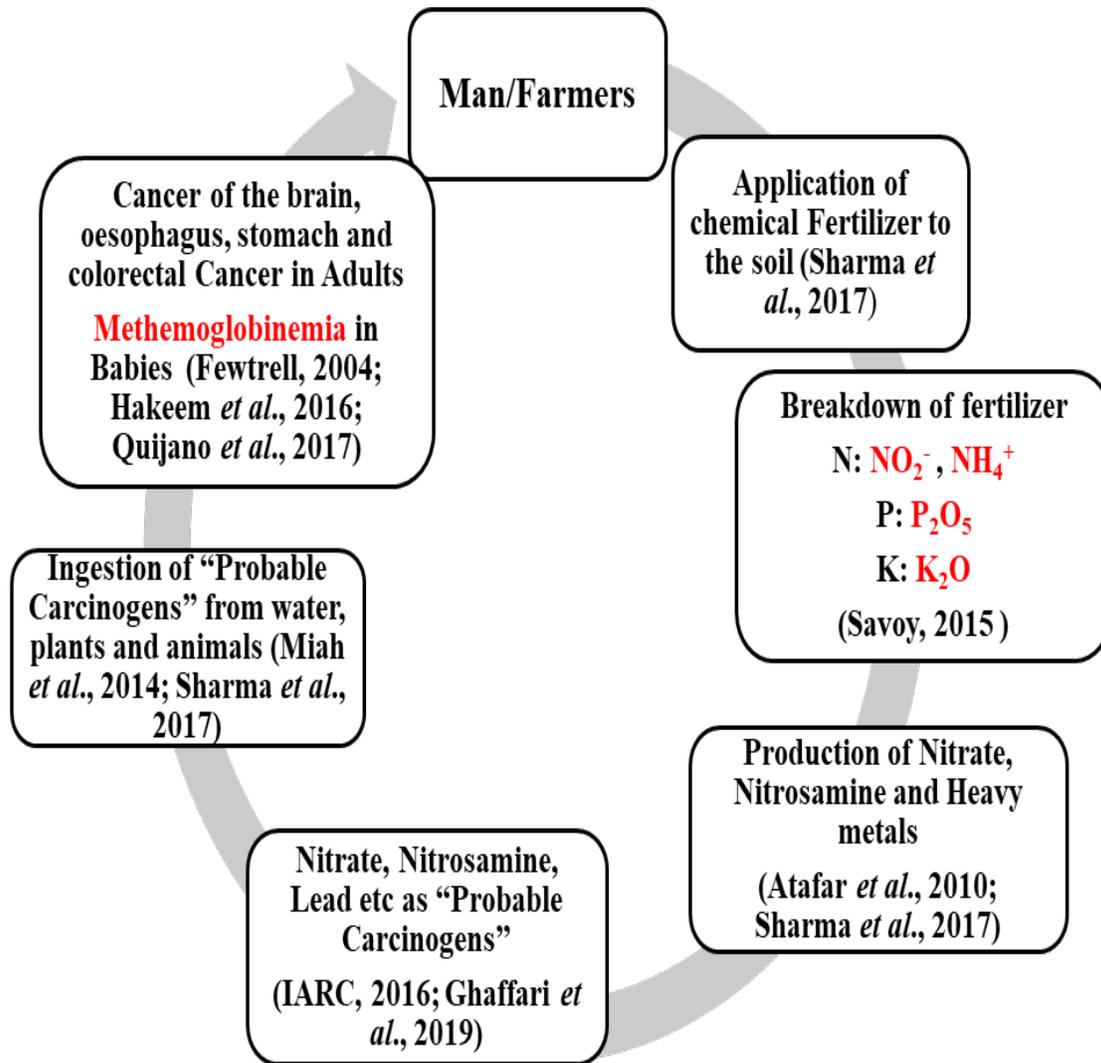


Figure 2: Possible Ways in Which Chemicals Fertilizers Cause Cancer

3.9 Chemical Fertilizer and Colon Cancer

The International Journal of Cancer carried out studies and reported that nitrate in drinking water even in low levels of concentration have been correlated with an increased risk for colorectal cancer. These findings confirmed long-held suspicions that long-term exposure to nitrate — a common groundwater contaminant that primarily originates from agricultural fertilizers — may be linked to cancer risk. The risks by which the results are gotten from nitrate converted into carcinogens called N-nitroso compounds after ingestion. (Schullehner *et al.*, 2018). More Research studies should be carried out on the effects of Synthetic Fertilizer in cancer.

4. CONCLUSION

The use of Chemical Fertilizer has both advantages and disadvantages. But overtime, the disadvantages have been at an increased rate. Studies have proven that the compounds used in the production of these fertilizers contain heavy metals like; Arsenic, lead etc. and probable carcinogens like; Nitrates and Nitrosoamines. Due to this reason, researches and analysis have been done on how to improve plant growth, increase yield and also be health-friendly using Bio-fertilizers. The use of bio-fertilizers continuously helps in the improvement of the soil structure. (Staff, 2018)

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