Pesticides are widely used in agriculture to control a variety of pernicious organisms that spoil the crops. The positive aspect of application of pesticides renders enhanced crop productivity and drastic reduction of vector-borne diseases. On the other hand, we have also realized that agrochemicals have residual effect in the environment, causing substantial contamination of terrestrial ecosystems and poisoning human food. The chemical burden on the natural ecosystem has increased due to the industrialization of the agricultural sector. Pesticides promise successful prevention of harmful bugs but the dangers associated with their use have sadly exceeded their beneficial effects. There is ample evidence that some of the pesticides do pose a potential risk to humans and other life forms and lead to unwanted side effects on the environment and their long-term and indiscriminate use has resulted in severe health effects. Human beings, especially infants and children, are highly vulnerable to deleterious effects of pesticides due to the non-specific nature and inadequate application of pesticides. This article represents the effect of pesticides on human health from various sources and recommends some sound suggestions to decrease this impact.

Keywords
Pesticides, Human health, Natural ecosystem, Long-term use

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Introduction
Pesticide are poisonous chemical compounds or a combination of deliberately released substances into the environment to prevent, discourage, control and/or kill and destroy species of insects, unwanted plants, rodents, fungi or other harmful pests. Pesticides are used to destroy, and damage, the pests and insects that attack crops. Different kinds of pesticides have been used for crop protection for centuries (Mahmood et al., 2015). Pesticides can be natural compounds or they can be synthetically produced. They may belong to any one of the several pesticide classes. The most widely used pesticides belong to the classes like organochlorines, carbamates, organophosphates, pyrethroids and neonicitinoids (Mahmood et al., 2015). Pesticides are widely used in agriculture to control a variety of harmful organisms that affect the crops (Osman et al., 2008).
In agriculture, pesticides are used for decreasing the losses caused by weeds, insects, microbial diseases and other agricultural pests in food production. Pests in the world today are destroying about 35% of all potential food crops before harvest. These losses mainly stem from insects, plant pathogens and weeds (Ghorab and Khalil, 2015). In the last century, Pesticides and agrochemicals have become an important part of the global farming system and showing a significant increase in crop yields and food production (Alexandratos and Bruinsma, 2012). Pesticides not only play vital role in agriculture but also in public health programmes and in urban areas to protect humans and plants against various diseases (Nicolopoulou-Stamati et al., 2016).

The positive aspect of application of pesticides gives enhanced crop productivity and drastic decrease in vector-borne diseases (Agrawal et al., 2010). On the other hand we have also realized that agrochemical have residual effect in the environment, causing substantial contamination of terrestrial ecosystems and poisoning human food (Carson, 1962). The chemical burden on the natural ecosystem has increased due to the industrialization of the agricultural sector. Pesticides are known to potentially cause a large number of negative health and environmental effects and their side effects can be an important environmental health risk factor (Nicolopoulou-Stamati et al., 2016). Every year about 5.2 billion pounds of pesticides are used worldwide, according to an estimate. The use of pesticides to mitigate pests has become a common practice worldwide. Their use is not limited to farming, but is often used in homes in the form of sprays, poisons and powders for controlling cockroaches, mosquitoes, rats, fleas, ticks and other harmful bugs. Pesticides promise successful prevention of harmful bugs but the dangers associated with their use have sadly exceeded their beneficial effects. Along with the targeted ones, non-target pesticides destroy plants and animals. Furthermore, with the passage of time some pests also develop genetic resistance to Pesticides (Mahmood et al., 2015).

The uncontrolled and indiscriminate application of pesticides has raised serious questions about the ecosystem as a whole and human health, bird and animal safety in particular. Despite the ban on application in many countries of some of the environmentally persistent and least biodegradable pesticides (such as organochlorines), their use is constantly on the rise. Owing to its rapid fat solubility and bioaccumulation in non-target organisms, pesticides pose significant health hazards to living systems. Pesticides may have many harmful effects even at low concentrations, which can be observed at biochemical, molecular or behavioral levels (Agrawal et al., 2010). The improper use of pesticides will contribute to biodiversity destruction. Most birds, marine species and livestock are endangered for their life by toxic pesticides. Pesticides are a problem for environmental protection and for global stability (Mahmood et al., 2015). There is ample evidence that some of the pesticides do pose a potential risk to humans and other life forms and lead to unwanted side effects on the environment (Igbedioh, 1991). Over time, pesticides have increased the quality of human safety by controlling diseases spread by vectors, but their long-term and indiscriminate use has resulted in severe health effects. Human beings especially infants and children are highly vulnerable to deleterious effects of pesticides due to the non-specific nature and inadequate application of pesticides. While the use of pesticides has risen in recent decades, the risk of exposure to such chemicals has also dramatically increased (Mahmood et al., 2015).
Materials and Methods

The present study is an attempt to focus the pesticide usage and its effects on human health. The design for the present investigation is descriptive research. The existing literature available in different sources is mapped for this purpose. The critical analysis of the research work done have been analyzed thoroughly and review of the same has been presented in results and discussion.

Results and Discussion

Around 2.2 million people, primarily from developing countries, are at greater risk of pesticide exposure (Hicks 2013). Each year about 25 million farm workers worldwide suffer accidental pesticide poisoning and it is estimated that around 1.8 billion people are involved in agriculture and most use pesticides to protect the food and commercial goods they generate. During the use of pesticides in sanitation campaigns and for lawn and garden applications, a few more people are occupationally exposed (Alavanja 2009). Additionally, some individuals are more prone to pesticide toxicity than others, such as babies, small children, farm workers and pesticide applicators (Mahmood et al., 2015). The majority of the farmers are unaware of the pesticide's possible toxicities. They have little or no information about types of pesticides, their level of poisoning, hazards and safety measures to be taken before use of those pesticides. Despite of this, harmful and biologically persistent chemicals are used to destroy pests and can also result in deliberate, accidental or occupational exposure. These compounds have long-term impact on human health (Sharma et al., 2012). The people who are at high risk and are more exposed to pesticides include production workers, formulators, sprayers, mixers, loaders and agricultural farm workers. The probability of hazards can be higher during manufacture and formulation, since the procedures involved are not risk-free. Workers are at increased risk in industrial settings, as they handle various toxic chemicals including pesticides, raw materials, toxic solvents and inert carriers (Aktar et al., 2009). Pesticide exposure and poisoning are a major problem among Indian farming communities. Exposure and poisoning not only pose a danger to farmers but also to farm laborers, women, children and consumers. Among all, pregnant women and children are the most vulnerable groups, when they work with pesticides in the field, working in sprayed fields, moving along or playing near sprayed fields, and through food and drinks contaminated by taking pesticide residues (Kumar and Reddy, 2017). People living in agricultural areas have a more exposure of pesticides by inhaling spray blows of pesticides in urban areas and parks or in homes after breathing contaminated air. Farmers and their families may be exposed to pesticides more than the general population (Allsop et al., 2015).

Human health effects are caused by

Skin contact: handling of pesticide products

Inhalation: breathing of dust or spray and

Ingestion: pesticides consumed as a contaminant on/in food or in water.

Farm workers have significant risk associated with inhalation and skin contact risks when handling and applying pesticides to crops. However, the main source for the majority of the population is food ingestion that is contaminated with pesticides (Agrawal et al., 2010).

Absorption of pesticides through skin and respiratory routes

The reports available indicate that the infants and children absorb more pesticides and their
residues, insect repellents and pediculocides than the adults through their skin and produce toxicity (Hallberg, 1989). This contributes to changes in behavior patterns and multiple syndromes of diseases such as encephalopathy, ataxia, seizures, muscle cramps, excessive urination and coma (McConnell, 1993). But, by applying these chemicals into the fields, farmers are usually exposed to pesticides. The absorption of pesticides by cutaneous and respiratory routes in farmers mainly contributes to the overall toxicity of the pesticides that have been reported to cause non-Hodgkins lymphoma (Hoar and Blair, 1886).

In recent decades, research has been focused on the determination and concentration levels of OCPs in human blood serum, maternal and cord serum, adipose tissue, human milk and hair and other tissues suitable for human exposure analysis and health risk assessment (Song et al., 2013). Human exposure to OCPs occurs through several routes like breathing OCP-contaminated air, working or living next to OCP factories, drinking and bathing with OCP-contaminated water, eating OCP-contaminated vegetables and grains, and eating fish and animal meats in particular (Wang et al., 2013). OCPs accumulated in the human body may cause various adverse effects such as harm to immunological function, endocrine disruption, spontaneous and preterm female abortions, and neurodevelopmental delays in children (Cioroiu et al., 2010).

Many staff and residents, especially in the rural sector, are in daily contact with pesticides, so these compounds pose a high risk of poisoning. This exposure can induce neuropsychiatric sequelae (mood disturbances, depression and anxiety), as certain pesticides underlie changes in central, peripheral, and autonomic nervous system function (e.g., cholinergic crisis), which are often accompanied by suicide attempts (Freire and Koifman, 2013). In agricultural production organophosphate compounds (OCs) and Organochlorine pesticides (OCPs) have been extensively used. They have proven to be highly dangerous to human health. OCs and other pesticides which are deleterious to the ecology may persist on Earth for a long time. Residues of pesticides in vegetables, fruits, water, and on Earth are therefore increasingly attracting attention (Shi et al., 2015). Organophosphate and carbamate toxicity is causing symptoms close to those of elevated neurotransmitter-acetylcholine. Such pesticides interfere with normal transduction of the nerve signal, and their exposure induces headaches, dizziness, anxiety, nausea and vomiting, muscle and chest pain. In severe cases, breathing difficulties, convulsions, coma and death can occur (Mahmood et al., 2015). In addition to causing tremors and seizures, pyrethroids may induce an allergic skin reaction, aggressiveness, over-excitation, reproductive or developmental effects (Lah, 2011). It is found that pesticides and Parkinson's disease and Alzheimer's disease are linked (Casida and Durkin, 2013). The National Institute for Occupational Health (NIOH) has assessed the magnitude of the toxicity risk involved in spraying methomyl, a carbamate insecticide, in field conditions (Saiyed et al., 1992). Significant changes were noted in the spray men in their ECG, the serum LDH levels, and cholinesterase (ChE), indicating the cardiotoxic effects of methomyl. Observations confined to health surveillance in male formulators engaged in the manufacture of dust and liquid formulations of specific pesticides (malathion, methyl parathione, DDT and lindane) in industrial settings in the informal sector indicated a high incidence of generalized symptoms (headache, nausea, vomiting, exhaustion, skin and eye irritation) in addition to psychological, neurological, cardiovascular symptoms (Gupta et al., 1984).
Degradation of water quality by the runoff of pesticides has two major impacts on human health. The first is the consumption of pesticide-contaminated fish and shellfish; this can be a particular problem for subsistence fish economies which lie downstream of large agricultural areas. The second concerns the overt use of water polluted with pesticides (Agrawal et al., 2010). The WHO (1993) has drawn up recommendations for 33 pesticides on drinking water. Many health and environmental protection agencies have set Acceptable Daily Intake (ADI) and Maximum Contamination Level (MCL) values which indicate the maximum permissible daily intake of pesticides over a person's lifetime without significant risk to the individual.

Acceptable Daily Intake (ADI)

It is used to establish a negligible residue level for pesticide tolerances on human food or animal feed products. This term has been now replaced by another term, negligible residue. Negligible residue means any amount of a pesticide chemical remaining in or on a raw agricultural commodity or group of raw agricultural commodities that would result in a daily intake regarded as toxicologically insignificant on the basis of scientific judgment of adequate safety data (Agrawal et al., 2010).

Maximum Contaminant Level (MCL)

This term refers to toxic chemicals regulated as contaminants under the Safe Drinking Water Act (SDWA). Although MCLs do not apply to pesticides specifically, they apply in a general sense. Under SDWA, pesticides are grouped with a larger collection of toxic chemicals that can affect human health when found at certain specific concentrations above established MCLs in drinking water. The Safe Drinking Water Act and the associated regulations try to prevent contamination of drinking water from reaching MCLs through continuous monitoring of water supplies. Regulations under the SDWA establish MCLs in much the same way as FIFRA, FDCA, and the Food Quality Protection Act of 1996 establish pesticide tolerances with negligible residues (Agrawal et al., 2010).

The effects

Repeated exposure to several pesticides and blends can have several complex health implications. Both the active ingredients and other inert ingredients in the pesticide formulation can also cause harmful effects (Kumar and Reddy, 2017).

Cholinergic effects

The cholinergic effects brought about by repeated administration of less than a single fatal dose are similar in type to the acute single-dose effects (WHO, 1986).

Acute toxicity

Acute toxicity is a substance's potential to cause adverse effects shortly after a single exposure or dosage, or any significant toxicity resulting from a single short-term exposure to a toxic substance. LD50 (lethal dose 50) is defined as the dose that kills 50% of a population of the tested animals (Ghosh and Philip, 2006). Pesticides can cause immediate health effects, such as headache, itching, nausea, vomiting, and fatigue and unconsciousness once within the body. Immediate effects of pesticide exposure involve eye and skin stinging, nose and throat inflammation, skin itching, dizziness, diarrhoea, stomach discomfort, nausea and vomiting, blurry vision (Mahmood et al., 2015).

Chronic toxicity

Pesticides' cumulative effects are often fatal, and may not even surface for years. These are
long-term effects causing damage to different organs in the body. Exposure to pesticides for extended periods of time results in the following consequences: a range of neurological health risks, such as loss of coordination and memory, decreased visual capacity and reduced motor signaling (Lah 2011).

Chronic toxicity is a substance's capacity to inflict adverse long-term or prolonged effects on health. Numerous studies have shown atrazine's chronic toxicity on different test species. After the sign of breathing difficulty and limb paralysis, 40 per cent of rats died for 6 months at an oral atrazine dosage of 20 mg / kg / day (Ghorab and Khalil, 2015).

Long-term exposure to pesticides affects the immune system (Culliney et al., 1992) and may result in hypersensitivity, asthma and allergies.

Residues of pesticides were detected in cancer patients’ bloodstream as compared with normal individuals. Pesticides have been related to leukaemia, lymphoma, brain, breast, prostate, ovaries and testes cancer (Mahmood et al., 2015).

The presence of pesticides in the body for longer periods often impacts the reproductive ability by manipulating the levels of reproductive hormones in males and females. This leads to stillbirth, birth defects, spontaneous abortion and infertility (Mahmood et al., 2015).

Long-term pesticide exposure often affects the liver, lungs, kidneys and can lead to blood disorders (Kumar and Reddy, 2017).

Delayed neuropathic effects

Delayed neuropathy has occurred occasionally in human being, livestock and experimental animals after intoxication with a variety of organophosphorus esters. However, many organophosphorus pesticides that might, theoretically, cause neuropathy, would only do so at a dose far above the lethal dose (WHO, 1986).

Some pesticides lead to long-term impacts on the health including nervous system injury and dysfunction, immune system, hormone system, reproductive system etc. These impacts can contribute to diseases and disorders such as behavioral changes, learning disabilities, Attention Deficit Hyperactivity Disorder (ADHD), autism (Kumar and Reddy, 2017).

Mutagenic and carcinogenic effects

Several organophosphorus pesticides in animal studies have not shown carcinogenic potential, but certain pesticides have, through induction of tumors in rats and mice. Since certain compounds exhibit mutagenic behavior, generalizations cannot be made, whereas other compounds do not (WHO, 1986).

Reproductive effects

There are a range of pesticides which can cause reproductive toxicity in animals and some Compounds are known to affect human reproduction (Sameeh, 2004). Also OPs included insecticides (malathion, parathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion), nerve gases (soman, sarin, tabun, VX), ophthalmic agents (echothiophate, isoﬂuorophate), and antihelmintics (trichlorfon). Herbicides (tribufos [DEF], merphos) are tricresyl phosphate– containing industrial chemicals.

OCP exposure may also have adverse effects on human health, including involuntary and premature abortions (Saxena et al., 1981),
delayed neurodevelopment during childhood (Eskenazi et al., 2006), and man reproductive disorders (Dalvie et al., 2004) and other adverse effects. As the rapid growth and development occurs in the fetus during early development, the baby's organs may be sensitive to the toxic substances (Weiss, 2000). Increasing evidence suggests that prenatal pesticide exposure may have a permanent effect on children’s behavior and intelligence (Munoz-Quezada et al., 2012).

Nursing mothers and pregnant women who are exposed to pesticides could also expose their children. Some pesticides may pass through the placenta to the growing fetus in the womb and into the breastfeeding infant through breast milk (Allsop et al., 2015).

Reduced sexual and reproductive development, reduced sperm counts, infertility, miscarriages, endometriosis; early puberty, abnormal menstrual cycle, early c. child birth, birth defects (Kumar and Reddy, 2017).

**Immunotoxicity**

Scientific evidence suggests many pesticides are damaging the immune system. Animal experiments have shown pesticides change the normal structure of the immune system, disrupt immune responses and that the resistance of animals to antigens and infectious agents. For example in case of Malathion which is considered a very low toxic compound (oral LD50 = 2100 mg/kg bw) for example, does not regulates the immune system, especially affecting non-specific immune mechanisms (Sameeh, 2004).

**Cytogenetic effects**

Cytogenetic risk associated with exposure to pesticides has been identified in different populations. Some researchers reported important variations in the percentage of chromosomal aberrations (CAs) in exposed individuals (range, 2.66–10.30%) compared with control (range, 0.53– 5.52%) (Sameeh, 2004).

**Cancer and Immunosuppression**

Studies have shown that exposure to pesticides greatly decreases resistance to bacterial, virus and parasite Infections and promote tumor development in many species of animals. Individuals exposed to pesticides have an increased chance of developing those cancers which are considered to be associated with immune suppression. In short, pesticides can affect a variety of cancers through an immunological mechanism (Sameeh, 2004).

**Effects on the immune system**

Most organophosphorus pesticides induce allergic reactions and inhibit development of antibodies (Zackov, 1983). Low-dose exposure is widely associated with human health effects such as immune suppression, disturbance of the hormones, reduced intelligence, reproductive defects and cancer (Brouwer et al., 1999).

Studies have shown evidence of pesticide exposure and disturbances in both hormonal imbalance control and immune system function. The statistical findings apply to the use to pesticides and the emergence of such diseases. The result cannot be ignored. The mechanisms of the diseases caused by pesticides are not yet fully known, but we now know some important enzymatic activities in main metabolic pathways and/or the permeability of the ion channels are affected by them (Mostafalou and Abdollahi, 2013).

**Effects on tissue carboxyesterase**

There are a variety of carboxyesterases abound in liver, intestine and other tissues.
The inhibition of one particular carboxyesterase has toxic sequelae, it has shown no direct deleterious effects of inhibiting other carboxyesterases. They may also contribute significantly to the metabolic disposal of malathion and many other organophosphorous pesticides, in order to inhibit tissue carboxyesterases may potentiate the toxicity of such pesticides (WHO, 1986).

**Hormonal disruption**

Scientific work has shown that many pesticides are endocrine disruptors that can interfere with the functioning of different hormones in the body (Mandrich, 2014).

The production of thyroid hormone is thought to be inhibited by substances such as cyhalothrin, amitrole, pyrimethanil and fipronil. Other pesticides may also alter thyroid hormone levels and potentially cause thyroid disease. Experimental studies *in vitro* support observations that the balance of sex hormones can be disrupted by exposure to certain pesticides. There is also evidence that fertility of both women and men may be decreased with increased pesticide exposure (Allsop *et al.*, 2015).

Many environmental chemicals, including pesticides known as endocrine disruptors, are considered to have harmful effects by imitating or antagonizing natural hormones in the body, and their long-term effects have been postulated (Brouwer *et al.*, 1999).

In conclusion, pesticides have proved to be a blessing for both farmers and people across the world by raising agricultural production and indirectly delivering countless benefits to society. Pesticides are often seen as a quick, easy and cheap solution to control weeds and insect pests in urban landscapes. However, pesticide use comes at a significant cost. Almost every part of our world has been polluted by pesticides. Residues of pesticides are found in soil and air, and in surface and ground water throughout the world, and uses of urban pesticides add to the problem. But the question of hazards to human health and the environment posed by pesticides has raised questions about the safety of pesticides.

**Suggestions**

While we can't eradicate the hazards associated with pesticide use entirely, we can mitigate them in one way or another. Exposure to pesticides and thus the adverse results and unintended effects of this exposure can be reduced by many means such as alternate crop methods or by using well-maintained spraying equipment. Also, natural control agents, such as beneficial bacteria, viruses, insects, and nematodes, can be used in improving crop protection successfully thus making better, safer and more friendly environment. Protecting crops through a multi-level approach will help us increase the variability of agricultural areas, providing a natural habitat for pollinators and species that control natural pests. The farmers who are the direct users of the pesticides should also be made aware of the right doses, proper safety measures, waiting period and harmful effects of the pesticides.

The havoc can be curbed if a less toxic formulation or a reduced dose of a toxic formulation is used. Reducing the use of pesticide strategies won't help us protect human health, as there are huge types of pesticides to be sold in the market. In this situation, people need to move for environmentally sustainable farming. This is a critical act to avoid all the risks involved. It is important to communicate the message that prevention of adverse health effects are beneficial investments for employers and workers as a contribution to a sustainable economic growth. There is therefore a need to
create and disseminate health education packages based on awareness, aptitude and experiences to reduce human exposure to pesticides within the population.

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