CHAPTER 1

INTRODUCTION

1.0 INTRODUCTION

Agriculture is the mainstay of the Indian economy. Because of the nature of farm work, farmers are at risk of developing a number of health problems. In the development of agriculture, pesticides have become important crop-protection agents for boosting food production. Exposure to pesticides, mainly the anticholinesterase-like organophosphates (OPs), both occupationally and environmentally, cause a range of human health problems (Kesavachandran et al., 2009). Currently, three million people are exposed to organophosphate pesticides yearly, with 3,00,000 adverse health outcomes-related to agricultural farmers (Perwitasari, Prasasti, Supadmi, Jaikishin, &Wiraagni, 2017). Developing countries use only 20% of the world's agrochemicals, yet they account for the 99% of death due to pesticide poisoning (Kesavachandran et al., 2009). Twenty-five million, agricultural farmers in the developing world suffer from at least one annual episode of pesticide-poisoning each year (Malekirad et al., 2013). Farming populations exposed to pesticides suffer from several health problems, primarily neurological abnormalities, respiratory ailments and dermal problems (Kesavachandran et al., 2009).

According to the latest reports, globally, nearly 3 billion kg of pesticides are used every year with a budget of ~40 billion USD. This extensive usage has increased the crop yield as well as led to significant reduction in harvest losses and thereby, enhanced food availability. On the other hand, indiscriminate usage of these chemicals has led to several environmental implications and caused adverse effects on human health. OPs are cholinesterase-inhibiting chemicals, predominately used as pesticides. OPs contain phosphorous derived from phosphoric acid and are generally the most toxic pesticides to the vertebrate animals (Lang, Zhu, & Zhang, 2012). OPs and carbamates inhibit the function of carboxylic ester hydrolases, such as chymotrypsin, acetylcholinesterase (AChE), plasma or butyrilcholinesterase (BuChE), plasma and hepatic carboxylesterases (aliesterases), paraoxonase (asterases), and

other nonspecific esterases within the body (Abdollahi, Ranjbar, Shadnia, Nikfar, &Rezaie, 2004). The most prominent clinical effects of poisoning with OPs result from the inhibition of AChE. Agricultural farmers are exposed to pesticides through occupational or environmental exposure during mixing, loading, transporting, and applying pesticides.

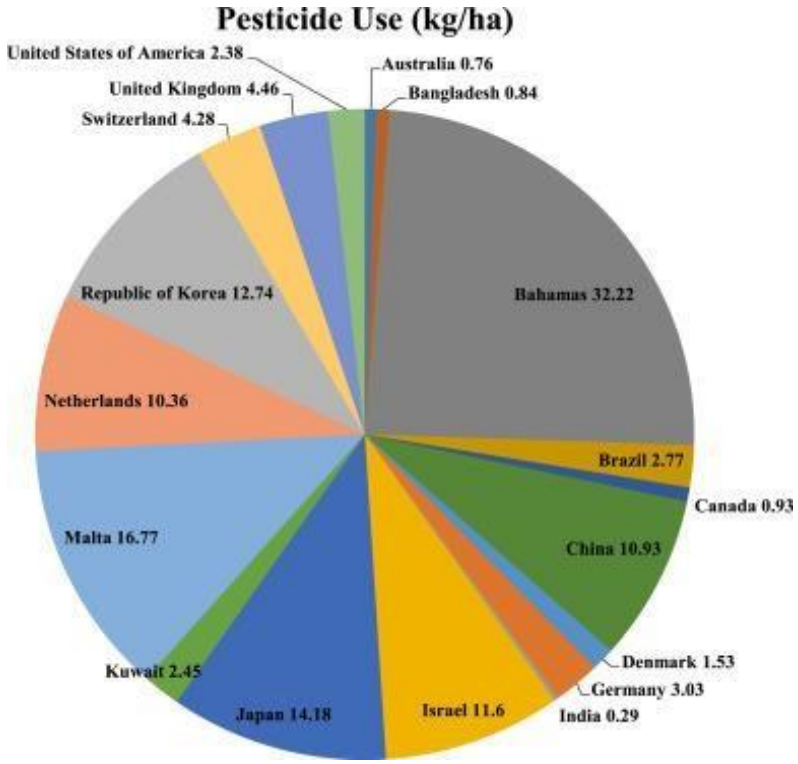

Figure 1: Global Trends in Pesticides

Pesticide exposure and handling

Worldwide, agricultural workers are prone to dire health implications due to acute and chronic exposure to pesticides (Damalas and Koutroubas, 2016). Several reports have suggested that, farmers are more susceptible to neurological, digestive, retinal, respiratory and reproductive disorders than general population, due to their close contact with these chemicals (Fuhrimann et al., 2019). Thus, it is important to take certain precautions to minimize the hazardous impact of these toxic substances on individuals involved in agriculture. One of them is extensive usage of personal protective equipment (PPE), which includes gloves, masks, protective goggles, boots, hats and respirators. Also, the applicator used for pesticide spraying should be in a suitable working condition and free from leakages (Damalas et al., 2016).

Effect of Organophosphates on human physiology

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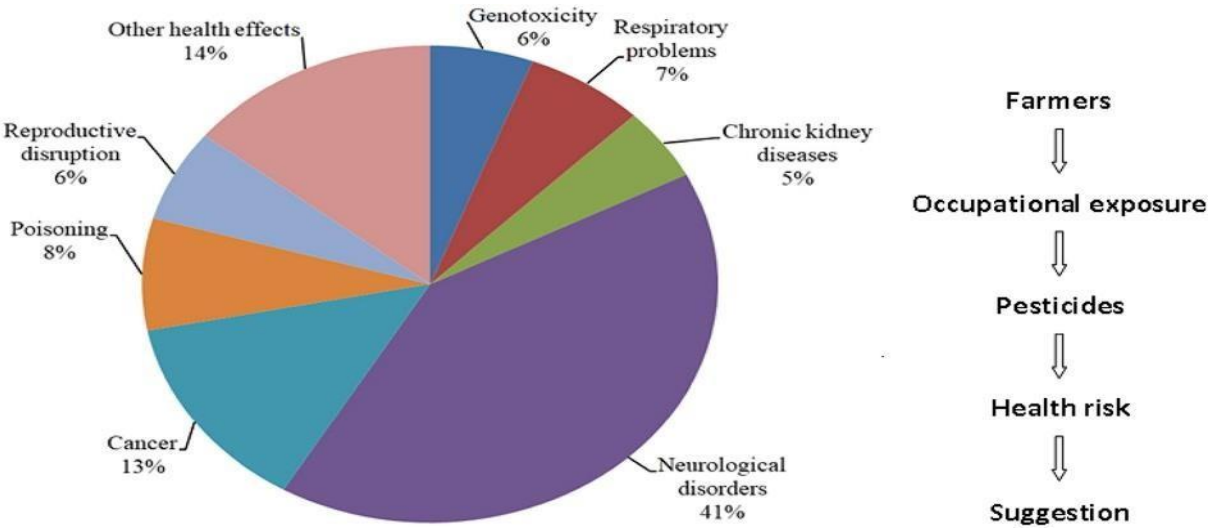

Figure 2: An overview of pesticide exposure and health hazards

OPs and carbamates inhibit the function of carboxylic ester hydrolases and other nonspecific esterase within the body within the body (Abdollahi, Ranjbar, Shadnia, Nikfar, &Rezaie, 2004).

Mechanistically, OPs have been defined as inhibitors of acetylcholinesterase (AChE). However, non- cholinergic targets of OP have also been documented (Teimouri et al., 2006), such as acyl peptide hydrolase, a serine proteinase. OP agents irreversibly bind and inhibit AChE, leading to a persistent increase in cholinergic stimulation. This produces acute effects of OP poisoning, including miosis, excessive secretions, seizures, severe muscle paralysis, cardiorespiratory depression, coma, and death. Primary intervention entails amelioration of the symptoms arising owing to the specific interaction of the pesticide with cellular targets. These interventions include treatment against acute symptoms of toxicity by treatment with anticholinergic drugs, such as atropine, oximes that reverse the AChE inhibition, and antiseizure drugs, such as midazolam.

Secondary interventions target the delayed injury responses and long-term neurological consequences of exposure to these agents with neuroprotective agents. Cholinesterase inhibiting agricultural pesticides in India is associated with a reduction in lung function, COPD, and a rise in respiratory problems (Chakraborty et al., 2009). Organophosphates exposure is significantly related to neurological or neuropsychological impairment (Steenland et al., 1994). Significantly, there is a decrease in AChE and BuChE activities in pesticide-exposed farmers (Dutta & Bahadur, 2018). Chronic toxicity effects of OPs are associated with the production of free radicals. Farmers exposed to pesticides are prone to oxidative stress (Ranjbar et al., 2002). Humans exposed either acutely or chronically to OP compounds develop similar oxidative stress indices, including decreased antioxidant capacity, free radical-mediated DNA damage, and free radical-mediated lipid peroxidation (Pearson & Patel, 2016). Principally, oxidative stress in human may result from diminished anti-oxidants or increased production of reactive oxygen species, which leads to lipid peroxidation (Ranjbar et al., 2002).

Pesticide use is an integral measure for agricultural sustainability, one of the key aims of the second sustainable development goal (SDG-2). However, the large-scale use of pesticides

has surfaced as a double-edged sword, associated with a varying range of detrimental health outcomes. The adverse respiratory consequences, particularly lung function decline, have been widely documented and have also been a major focus of the National Institute of Occupational Safety & Health (NIOSH). Reductions in spirometric variables (FEV1, FEF25-75%, and FEV1/FVC%) and respiratory illnesses seem to be the widely associated outcomes of chronic exposure to pesticides. Cognitive impairment is another major predominant adverse effect of chronic pesticide exposure, which could lower the well-being of farmers, an essential requisite for agricultural sustainability. Given the fact that illiteracy substantiates the risk of pesticide exposure, implementation of educational strategies is one of the most appropriate preventive measures. However, the high magnitude of lung deterioration noted even within a short span of 4 years of pesticide exposure also demands early clinical interventions to reduce further exacerbations.

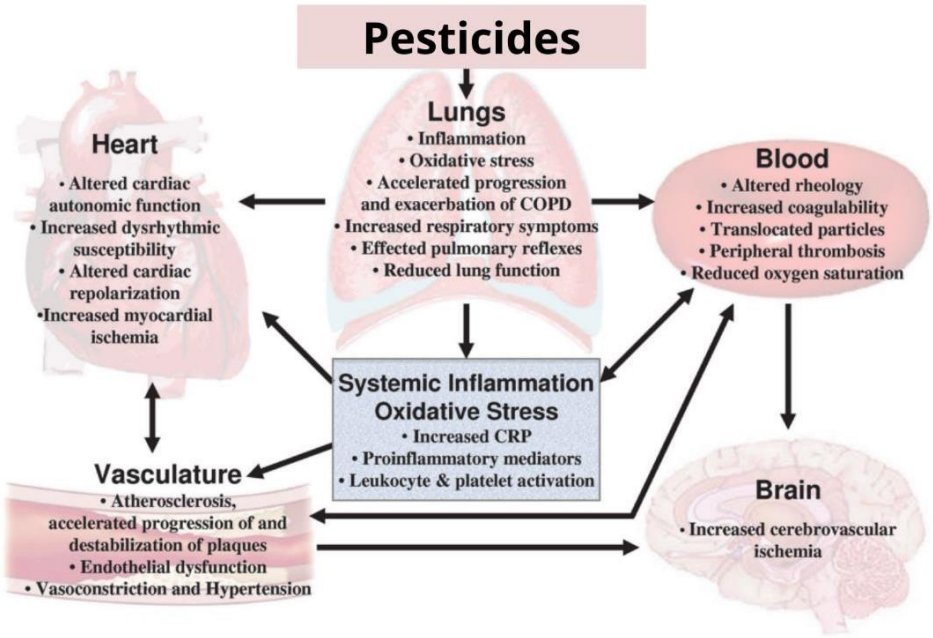

Figure 3: Pesticide exposure, oxidative stress, and deterioration of different organs

Yoga is a multi-component mind-body intervention; meta-analyses of its reports support the improvement in respiratory parameters in various clinical settings, including chronic

obstructive pulmonary disease (COPD) [FEV1, weighted mean difference (WMD): 123.57 mL, 95% CI: 4.12-243, P=0.04]. Cramer et al. highlight the specific potency of breathing-focused yoga (BFY) practice on pulmonary function in COPD. There has also been meta-analysed significant outcomes reported for cognitive benefits of yoga (g = 0.33, standard error = 0.08, 95% CI = 0.18-0.48). Yoga also improves cholinesterase and decreases MDA level, decreasing sympathetic activity and oxidant stress (Damodaran et al., 2002). There is a study that shows the positive effects of yoga on physical and respiratory functions healthy inactive middle- aged people (Yamamoto-Morimoto, Horibe, Takao, &Anami, 2019)

Over recent years, there has been increased recognition of evaluating hypothesized mediating mechanisms randomized trials. Furthermore, oxidative stress is one of the unanimous pathological mechanisms underlying pesticide-induced toxicity of varied pesticides; yoga has been priorly associated with alleviating imbalances in oxidative stress parameters. Hence, we aimed to test the mediating effects of the oxidative stress markers to establish the effectiveness of the yoga-based intervention.

We aimed to test the effectiveness of a yoga-based will be examined through a parallel-group randomized controlled trial with the above background. The primary aim of this study is to examine the efficacy of yoga intervention on the improvement of respiratory function in pesticide exposed farmers, operationalized as the absolute difference in the means of the spirometry parameters after three months of intervention compared to the waiting list control group. The secondary aim was to examine the efficacy with regard to cognitive function, quality of life, perceived stress, and a waiting list control group after treatment and during the follow-up period. In addition, we also aimed to investigate the mediating effects of oxidative stress markers that might underlie the hypothesized impact of the yoga-based intervention on the primary and secondary outcomes of the study. Finally, with the background of the effectiveness of yoga on respiratory and cognitive domains of health, we aim to evaluate the

effectiveness of yoga intervention on respiratory and cognitive health in Indian farmers chronically exposed to pesticides.

Under these settings, Yoga-based clinical interventions could serve as a practical and cost-effective solution for healthcare needs. Hence, we tested the effectiveness of yoga as an intervention in a randomized clinical trial of 6 months against respiratory and cognitive deficits in pesticide-exposed farmers against a wait-list control condition.