India has a large and diverse agriculture and is one of the world’s leading producers (MAP, 2007). Agriculture sector provides principal source of livelihood for more than 58% of the Indian population (DAC; Annual Report 2010-2011). Indian agricultural scientists and farmers have a great challenge to ensure food and nutritional security of national population, which is about 17.5% of world population, within a limited 2.3% world’s total land area (DAC; Annual Report 2010-2011). The introduction of high yielding variety of seeds like hybrid seeds, better water and soil management, use of modernized-farm techniques, fertilizers and introduction of new pesticides has considerably increased the food, fodder and fiber production of the country. But inappropriate and intensive use of pesticides leads to increased risk of exposure to pesticides among agricultural workers and general population through occupational exposure, pesticide-residual contamination in food commodities and poor environmental conditions (ITRC, 1990).

Pesticide means any substance or mixture of substances of chemical nature or biological origin which is intended for preventing, destroying, attracting, repelling, mitigating or controlling any pest including unwanted species of plants or animals during the production, storage, transport and distribution of agricultural commodities or animal feeds (The Pesticides Management Bill, 2008). The word ‘Pesticide’ also covers substances intended for use as plant growth regulator, defoliant, desiccant, fruit thinning agents, or sprouting inhibitor and substances applied to crops either before or after harvest to protect them from deterioration during storage and transport (The Pesticides Management Bill, 2008).

Pesticides are used to control/destroy pest in agricultural sector to achieve better quality and increase production of food, feeder and fiber. In health sector, it is used to control/eradicate vector borne diseases (Gupta, 2004). Beside this, pesticides are also used in personal, domestic, industrial purposes and also in building materials (Gupta, 2004).
Nearly half of the world’s labor or over 1.3 billion workers are engaged in agriculture sector and India along with China share over 60% of the world’s agricultural workers (Rice, 2000). Unsystematic use of pesticide in agricultural sectors without proper preventive measures leads to pesticide exposure among agricultural workers during mixing, loading and application of pesticides. They are generally exposed to pesticides through inhalation, ingestion and dermal routes of exposure. Occupational exposure to pesticides may be associated to increased health risks among pesticide sprayers (Pathak et al., 2011a; Fareed et al., 2010; Singh et al., 2007; Kesavachandran et al., 2006a). The workers at pesticide manufacturing units (Srivastava et al., 2000), or retail shops (Kesavachandran et al., 2009) are also at risk of exposure to these chemicals and carry increased health risks associated with pesticides. Occupational pesticide exposure may result in mild to severe pesticide poisoning episodes among the agricultural workers. The signs and symptoms like headache, dizziness, difficulty in breathing, excessive sweating and excessive salivation due to mild poisoning; nausea and vomiting in moderate poisoning; consciousness and seizure due to severe poisoning (Mancini et al., 2005). The signs and symptoms of pesticide exposure may be localized (burning/tearing of eyes, burning or runny nose) or systemic (excess sweating/salivation, dizziness, headache, blurred vision, muscle cramps, nausea, staggering, tremor, twitching of eyelids, vomiting, loss of consciousness and seizure). These signs and symptoms depend on the severity of exposure (Mancini et al., 2005).

Organophosphorus (OP) pesticides are extensively used in agricultural sector, due to broad spectrum and less persistent in the environment compared to organochlorines (OCs) (Gupta, 2004). Most of the OP pesticides are volatile at room temperature and their exposure may be either dermal or respiratory route and can produce adverse effects even with low-grade depression in cholinesterase (Gordon et al., 1991). Cholinesterase inhibition has an important step in toxicity of OPs. Individual susceptibility, alteration of other enzymatic systems and direct effects of OPs are also part of pesticide toxicity (Kamanyire et al., 2004). OP pesticides on exposure can cause a sequential triphasic illness
in population, starting with cholinergic phase, which progresses into intermediate syndrome and finally organophosphate-induced delayed polynueopathy (OIDP) (Kamanyire et al., 2004). The OP/carbamate (CB) pesticides inhibit the enzymatic activity of acetylcholinesterase (AChE) and butyrylcholinesterse (BChE) (Lessenger et al., 2001). AChE inhibition affects hydrolysis of acetylcholine (ACh) leading to ACh accumulation, constant ACh receptor triggering which affects the proper functioning of the autonomic, neuromuscular and central nervous system (Lessenger et al., 2001).

Acute OP poisoning leads to acute cholinergic syndrome characterized by muscarinic symptoms (salivation, tearing, sweating, bronchoconstriction, bradycardia, vomiting, blurred vision and gastrointestinal problems), nicotinic symptoms (muscle fasciculations, tremors, muscle weakness with respiratory failure, hypertension, tachycardia, mydriasis and flaccid paralysis) and symptoms like headache, insomnia, giddiness, confusion, slurred speech, convulsions, coma and respiratory depression related to central nervous system (Aardema et al., 2008; Kamanyire et al., 2004).

Chronic pesticide exposure is a problem in occupational/environmental settings, especially for workers who work and live in close proximity to pesticide treated fields (De Silva et al., 2006) and direct re-entry of workers in field soon after spraying (Rastogi et al., 2008). Chronic toxicity may be related to the rate of regeneration of AChE and the rate of hydrolysis and elimination of pesticide metabolites from the body (De Silva et al., 2006). Chronic toxicity can result in adverse health events in pesticide sprayers (Pathak et al., 2011a; ITRC, 1990) in factory workers (Srivastava et al., 2000), in pesticide retail shopkeepers (Kesavachandran et al., 2009) and in children (Rastogi et al., 2010). Impairment of neurobehavioral performance like anxiety disorder, depression, psychotic symptoms, problems associated with memory, learning, attention, information processing, eye hand coordination and reaction time may also be associated with chronic exposure to OPs (De Silva et al., 2006). Studies on chronic OP exposure on nerve conduction and neuromuscular transmission are inconclusive (De Silva et al., 2006). Some studies showed effect of
pesticide exposure on nerve conduction abnormalities (Pathak et al., 2011b; Peiris-John et al., 2002; Ruijten et al., 1994). Chronic pesticide exposure also leads to adverse subclinical changes among population exposed to pesticides. Subclinical changes such as significant cholinesterase inhibition (Rastogi et al., 2008; Singh et al., 2006), peak expiratory flow rate (PEFR) decrement (Kesavachandran et al., 2006b; Rastogi et al., 1989), hematological alterations (Fareed et al., 2010) and slowing of nerve conduction velocity (Pathak et al., 2011b) were reported due to occupational exposure to pesticides. These subclinical changes due to pesticide toxicity are either irreversible or reversible.

Malihabad, a block in Lucknow District of North India, is famous for mango production. India ranks first in the world and accounts for 57.18% of the total world mango production (Kesavachandran et al., 2006a). Spraying of pesticides was conducted during December-March in mango orchards to combat against the pest. Thus, pesticide sprayers engaged in the spraying operations are directly exposed to different classes of pesticides, predominantly OPs like monocrotophos, chlorpyrifos, phorate, malathion, chlorfenvifos, endosulfan and methyl parathion. The farmers are also actively engaged in pesticide spraying in agricultural crops like wheat, rice and vegetables at Bakhshi Ka Talab, Lucknow District. They are also engaged in medicinal farming like menthol farming. Most of workers apply OP/CB to protect their crops or vegetables and thereby exposed to mixture of pesticides.

Pesticides like OP and CB are also known as anticholinesterase pesticides and biomonitoring of cholinesterase (ChE) activity is good indicator for assessment of exposure to these pesticides (Hofmann et al., 2009). Butyrylcholinesterase (BChE) activity is more sensitive indicator of mixed exposure of pesticides (Richter et al., 1992). Cholinesterase inhibition and pesticide related morbidity profile among population occupationally exposed to pesticide have been reported in studies from India (Pathak et al., 2011a; Chakraborty et al., 2009; Rastogi et al., 2008; Singh et al., 2007; Naravaneni et al., 2007; Kesavachandran et al., 2006a; ITRC, 1990), Nepal (Atreya et al., 2012),
Thailand (Jintana et al., 2009), Ghana (Ntow et al., 2009), Saudia Arabia (Al-Sarar et al., 2009), Peru (Catano et al., 2008) and Sri Lanka (Smit et al., 2003). Pesticide like pyrethroids (PY) affect the sodium channels of the nerve membrane leading to prolonged duration of opening of sodium channels across the nerve membrane (Fengsheng, 2000) and also act on some isoforms of voltage sensitive calcium and chloride channels (Sorderlund et al., 2002).

Pesticide exposure is associated with a range of symptoms as well as deficits in neurobehavioral performance and abnormalities in nerve function (Keifer et al., 1997) with increased risk of neurodegenerative disease, particularly Parkinson’s disease (Le Couteur et al., 1999). Neurotoxicity of pesticides can leads to axonal degeneration of peripheral nerves in lower limbs which may cause muscle weakness and degeneration in spinal cord, brain stem and cerebellum and may be associated with disturbance of coordination, vibration sensation, and balance (Sathiakumar et al., 2004).

A variety of neurological method like nerve conduction velocities, visual-auditory- and somatosensory- evoked potential, event related potential and computer-based posturography are used to evaluate subclinical neurophysiological alterations (Kimura et al., 2005). Neurophysiological studies are more sensitive for detecting subclinical nerve impairment even in asymptomatic workers (WHO, 1987) and in pesticide exposed population also (Pathak et al., 2011b; Kimura et al., 2005). Nerve conduction velocities (NCVs) and postural sway seem to be sensitive indicators for the pesticide toxicity related central and peripheral nervous system (Kimura et al., 2005). Nerve conduction studies categories neuropathy according to distribution (mononeuropathy, mononeuropathy multiplex or generalized), axonal v/s demyelinating and small v/s large fiber neuropathy (Misra, 2008). Motor/ sensory peripheral nerve defects, chronic neurobehavioral, deficits in verbal abstraction, attention, memory, anxiety and depression are some of the neurological effects related to pesticide toxicity (Pathak et al., 2011b; Hong et al., 2009; Farahat et al., 2003; ITRC, 1990).
A study of subclinical changes due to pesticide exposure in human population is often inconclusive. The role of different confounders for the slowing or deficits of nerve conduction in pesticide exposed population needs to be explored. Hence, the study was undertaken to assess the nerve conduction velocity, cholinesterase activity and pesticide exposure related self reported symptoms among agrarian/retail shopkeepers. The study is unique in the sense that in developing countries like India, mixed pesticide use is rampant and farmers spray pesticide without taking correct personal protective equipment (PPE). The cause–effect relationship and mechanism of action evolved from this study can be helpful in formulating a health management plan for agrarian/industrial population exposed to mixed pesticides and thereby improve work practices.

**Aims and Objectives**

1. Assessment of the effects of exposure to mixed pesticides on health status of workers.
3. Assessment of the effects of exposure to mixed pesticides on acetylcholinesterase activity and butyrylcholinesterase activity.
4. Assessment of the effects of exposure to mixed pesticides on nerve conduction velocity.
5. To explore the factors associated with nerve conduction deficits.