European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 7, Issue 07, 2020

"Association of Cognitive function and Depression with Chronic exposure to Organophosphate pesticides in the Agricultural community of rural area of Wardha District."

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STUDY PROTOCOL

Conflict of Interest: None

Funding: The study protocol will be submitted for ICMR grant and DMIMS Intra mural grant .

Abstract

A vast majority of India's population (58%), depends on agriculture for their livelihood and a vital part of our agricultural production technology constitutes of Pesticide use. According to a international report in 2013 " India is the largest producer of pesticides in Asia and ranks 12th worldwide for application of pesticides". In India ,Maharashtra has been the biggest consumer of pesticides in the last 5 years

Indian agricultural community belongs to the unorganized sector; hence they receive quite little in terms of healthcare and social security. They thus are very vulnerable to loss of income and unavailability of healthcare, despite belonging to an occupation which involves numerous hazardous possibilities.

Chronic exposure to organophosphate pesticides is associated with a multitude of ill health outcomes including polyneuropathy, dermatitis, behavioral changes, glucose intolerance & cancer .The Nervous system in particular in more sensitive to the Organophosphate pesticides, so monitoring of chronically exposed people may help prevent the onset of future neurodegenerative diseases.

The aim of this study is to assess changes in levels of Acetyl cholinesterase levels due chronic pesticide exposure, evaluate cognitive function and depression among farmers

chronically exposed to organophosphorus compounds, and determine the association between them.

Using standardized questionaries, data will be collected about personal habits, work practices, awareness of pesticide exposure adverse effects and among individuals living in area of study, involved in agriculture repeatedly in direct contact with pesticides. Blood samples to assess biomarker (cholinesterase) will be taken and cognitive function and depression assessment will be done using MMSE tool and PHQ-9 / Beck's inventory.

Data collected over study period will be analyzed and appropriate statistical tests will be used to determine results and draw relevant conclusions.

Key words: Chronic exposure; Organophosphate pesticides; Agricultural community; Acetyl Cholinesterase; Cognitive function; Depression; Cross-sectional study

INTRODUCTION

Farmers are the backbone of our country. Agriculture in India dates back to beginning of civilization here. Currently, India is 2nd highest in agricultural production in the world. Agriculture is the foremost occupation of India and the linchpin of our socio-economic growth. Furthermore, India is now aspiring to double our agricultural revenue by 2022. [1]

The Green revolution has given a undeniable thrust to agricultural progress and productivity. The agrochemicals made India competent, but their nonselective use has blighted our health, food and environment.[2]

On May 2020 The Ministry of Agriculture passed 'Banning of Insecticides Order, 2020' . This order puts a stay on the the production , sale , and use of 27 pesticides which have proven risk to health of humans and animals. This list of now banned pesticides belong to the highly hazardous group of pesticides as classified by WHO [3]

Pesticide poisoning is a pressing global health issue . In developing nations like India , Organophosphate pesticides are very economical and accessible, thus becoming a common cause for both intentional and accidental poisonings.

Despite the fact that the phenomenon of accidental poisoning due to chronic exposure because of negligence in practicing preventive measures during spraying/application is not entirely alien, only select few studies have been carried out on this . [4] The studies done on this subject have documented increasing incidence of ill-health symptoms like easy fatigability , insomnia , raised stress levels , headaches, irritable mood , depression , numbness in hands and feet in adults who were chronically exposed to pesticides.[5]'Suicide impulse' is a side effect of OP poisoning which may be a contributor to the increased incidences of suicides among the agricultural workers.[6]

Organophosphate pesticides lead to irreversible inhibition of cholinesterase in our bodies . While plasma pseudocholinesterase is preferred for measuring acute toxicity , blood cholinesterase levels give a better estimate for chronic exposure. Cholinesterase also is quite sensitive to low level residues due to chronic exposure in pesticide sprayers .

RATIONALE:

A report, by Factly media and research on States with high usage of pesticides , stated that "Among the Indian states , the net consumption of pesticides irrespective of area under cultivation is the highest in Maharashtra . Incidentally, Maharashtra also continues to report the highest number of suicides in the agricultural sector."[7]

The distinct symptoms of cholinergic crisis make the diagnosis of acute organophosphate poisoning relatively easy, but symptomatology of chronic exposure to organophosphate pesticides is evident only at a much later stage; when a lot of irreversible harm has already been done to the body. The nervous system is vulnerable to damage by chronic exposure to Organophosphate pesticides, thus making timely screening for neurological side effects in at-risk populations a necessary measure to prevent potential harm to the nervous system, by actively avoiding or cutting down the level of organophosphate use.[5]

Although detailed studies have been done on awareness of safety practices in pesticide application, and effects of acute organophosphate poisoning, there has not been much research on association of farmers mental health with chronic exposure to pesticides in Maharashtra. This study intends to explore and throw light on the neuropsychiatric effects of organophosphate pesticides on the farming community in Wardha district of Maharashtra.

AIM:

Our study aims to find out cholinesterase levels in blood among agricultural workers with chronic exposure to organophosphate pesticides and to study the association of cognitive functions and depression among them with cholinesterase level.

OBJECTIVE:

1. To find out the cholinesterase levels in blood, among agricultural workers with chronic exposure to Organophosphate pesticides from rural area of Wardha district

2. To assess to cognitive function and depression among agricultural workers from rural area in Wardha district.

3. To study the association of cognitive function and depression with cholinesterase level among agriculture workers from rural area in Wardha district.

Secondary objectives

1. To find out awareness of adverse effects of exposure to organophosphorus compounds and preventive practices for the same.

METHODOLOGY:

Study design: This will be a Cross-Sectional Study.

Study Settings: The field practice area of Department of Community Medicine, JNMC, Wardha will constitute the study setting for the proposed study.
Seloo taluka is one among the 8 talukas of Wardha district, Maharashtra. It belongs to Vidarbha region and is about 17 km east of the district headquarters, Wardha. Agriculture is

the mainstay of earnings for most inhabitants. Cotton and soyabean are the main crops cultivated here. Pesticides are used injudiciously in these areas. The men and women both are repeatedly/chronically exposed to organophosphate pesticides due to negligence in storage, purchase, mixing and application of pesticides.

Sampling procedure: Study participants from the selected villages will be selected though the Systematic Random Sampling

Study Participants: Any individual belonging to agricultural community of >30 yr. age, living in the selected villages from Seloo block of the Wardha District, for more than 6 years, and engage in the any farm work – own / as a daily wage laborer for more than 3 months will be taken as participation in our study.

Inclusion criteria: All Agricultural workers>30years, engaging in farm work and handling pesticides for more than 3 months.

Exclusion Criteria-

1**.** Study subject who does not give consent to take part in the study.

2.Study subject with pre-existing psychiatric comorbidities.

3.Study subject with history of acute organophosphorus poisoning.

Key outcome variables:

1.. Prevalence of chronic exposure to organophosphate pesticides measured by blood cholinesterase levels

2. Association of chronic exposure to organophosphate pesticides with cognitive function.

3. Association of chronic exposure to organophosphate pesticides with depression.

Data Sources/ Measurements:

Data will be collected through face-to-face interviews, using following pre-structured and pretested tools formulated in English. The tools will also be translated into Marathi, the native language for ease of collecting data from the community. The questionnaire will have 3 main segments.

1. Sociodemographic questionnaire - Socio-demographic profile of the Agricultural workers This will include personal demographic data ; occupational history of years of pesticide usage ; tobacco and alcohol consumption habits ; obstetric history in women .
2. MMSE examination scale – To assess the cognitive function.
3. PHQ –9 / Becks Depression inventory to assess depression.

The questionnaires will aim to collect the following information:

- Pesticide procurement, handling and storage practices .
- PPE usage practices while mixing and spraying pesticides

- Frequency and Nature of health adverse effects reported by Agricultural works after unprotected exposure to pesticides
- Cognitive function of the subjects.
- Presence and severity of Depression

Blood sample collection: Blood samples will be collected from consenting study participants and investigated for Cholinesterase levels, to quantify exposure to organophosphorus compounds over time.

Sample size:

Based on Sample size determination manual by S.K. Lwanga.

Taking Confidence level 90%, P [Anticipated population proportion]: 0.50, d=0.7

$$\mathbf{n= z^2_{1-x/2}P(1-P)/d^2}$$

Sample size = 138

Analysis plan:

Average cholinesterase level (with 95% Confidence interval) will be estimated. Cholinesterase levels will be compared across risk factors, demographic and social factors. Association of cholinesterase level with depression and cognitive functions will be assessed. Multivariate analysis will be conducted to study the predictive value of cholinesterase level on depression and cognitive function, controlling for demographic and social factors that were significantly associated with cholinesterase level in bivariate analysis. All analysis will be performed using the STATA Version 14 statistical software.

Expected Outcome/Results :

This study will help in determining the association of chronic exposure to pesticides with cognitive function and depression, if present.

This study will help us understand prevalent perceptions & practices in regards to insecticides /pesticides & PPE usage.

It will throw light on need for more stringent laws regarding use of organophosphorus containing pesticides, and promote use of biopesticides.

It will also help in sensitization of Agricultural workers in regards to hazards of insecticides /pesticides exposure, importance of PPE & help in reducing morbidities & mortality related to insecticides /pesticides usage.

Discussion:

A study by "Buralli, Rafael Junqueira et al" "Data on pesticide exposure and mental health screening of family farmers in Brazil." collected data from a rural area in Brazil . They used self reported questionnaire of WHO to screen for common mental disorders and did cholinesterase blood test to measure extent of pesticide exposure .[8]

A study by" Dhalla, A. S., & Sharma, S. " (2013) titled "Assessment of serum cholinesterase in rural Punjabi sprayers exposed to a mixture of pesticides." studied effect of pesticide

cocktail on pesticide sprayers of rural Punjab who were exposed to the these agrochemicals since childhood and concluded that serum cholinesterase is a good index of chronic low dose exposure to pesticides.[9]

A study by "Mathew, Philip et al" titled "Chronic pesticide exposure: Health effects among pesticide sprayers in Southern India." published in "*Indian journal of occupational and environmental medicine"* vol. 19,2 in 2015 , studied morbidity profile of pesticide sprayers in a rural Tamilnadu using questionnaires , pulmonary function tests , blood cholinesterase and peripheral sensations concluded that pesticide sprayers had higher morbidity than people of other occupations and serum cholinesterase was not a good measure for chronic exposure to pesticides.[10]

A study by "Serrano-Medina, Aracely et al" titled "Neuropsychiatric Disorders in Farmers Associated with Organophosphorus Pesticide Exposure in a Rural Village of Northwest México." published in "*International journal of environmental research and public health* vol. 16" in 2019 studied the mental state of agricultural workers using MINI questionnaire and analyzed cholinesterase levels via modified Ellman method . The results of their study threw light on need for preventive and functional strategies that teach farmers integrated pesticide management [11]. Evidences from Global Burden of Disease have been reported [12-15]. A number of related studies reflected on depression[16-20].

Key Results: The current study will determine

-Association of various levels of cholinesterase level with cognitive function and depression.

-Cognitive function and depression in farmers chronically exposed to pesticides.

-Limitations: This cross-sectional study will be conducted only in select villages of Wardha dist. Maharashtra. So, it cannot be generalized to other regions of the country; External validity is limited.

Conclusion: Conclusions will be derived based on data analysis.

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